SUPPORTING INFORMATION

Amphiphilic poly(aminoester) dendrimers: Click reaction-enabled synthesis, structure-governed self-assembling and degradation

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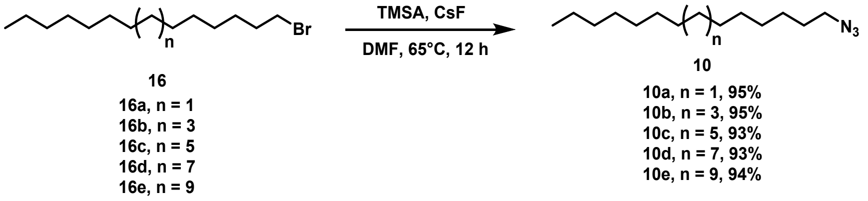
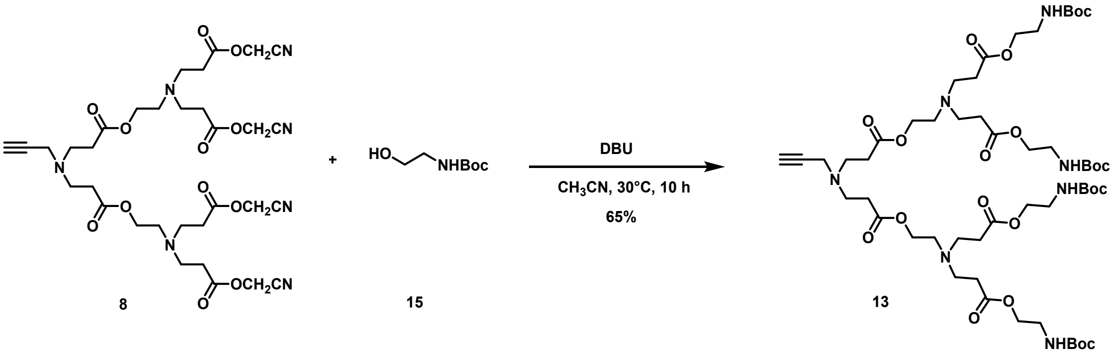
Supplementary Schemes

Scheme S1 Synthetic route to different hydrophobic moieties bearing an azido group (**10a-e**).

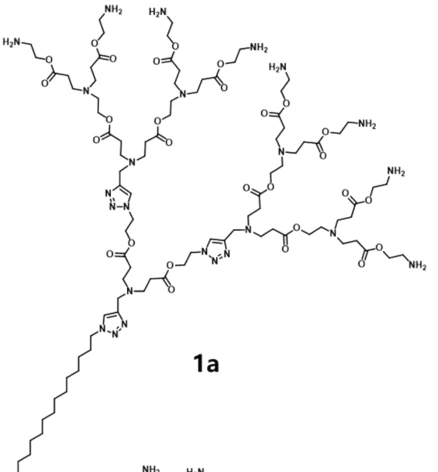


Scheme S2 Synthetic route to hydrophilic PAE dendron (**13**).

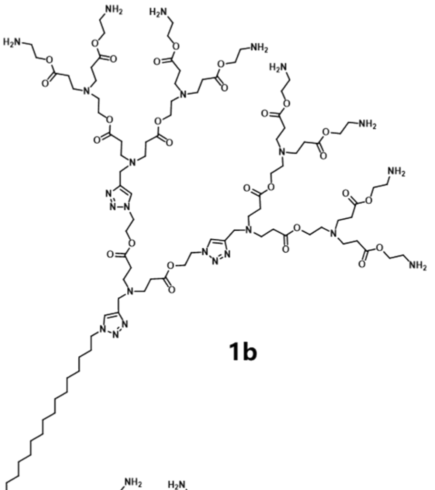


Supplementary Figures

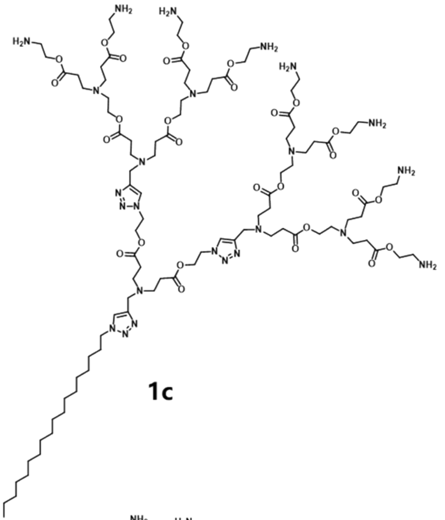
Figure S1 Chemical structures of amphiphilic PAE dendrimers (**1a-1e**) featuring hydrophobic lipid chains ranging from C_{14} to C_{22}.



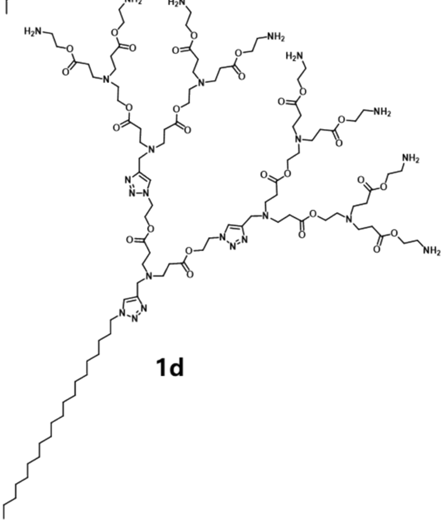
1a



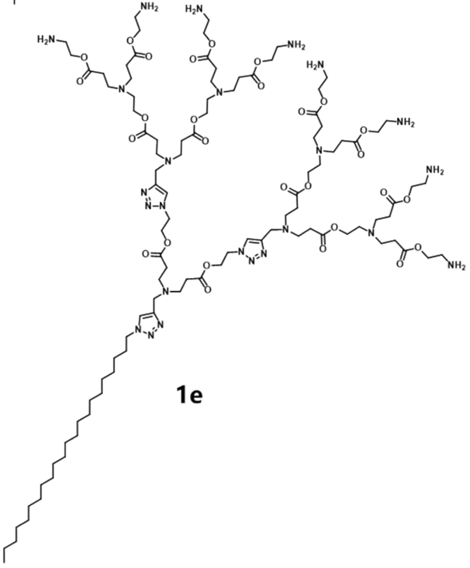
1b



1c



1d



1e

Figure S2 A) ^{1}H NMR, B) ^{13}C NMR, C) HPLC, and D) HRMS spectra of **1a**.

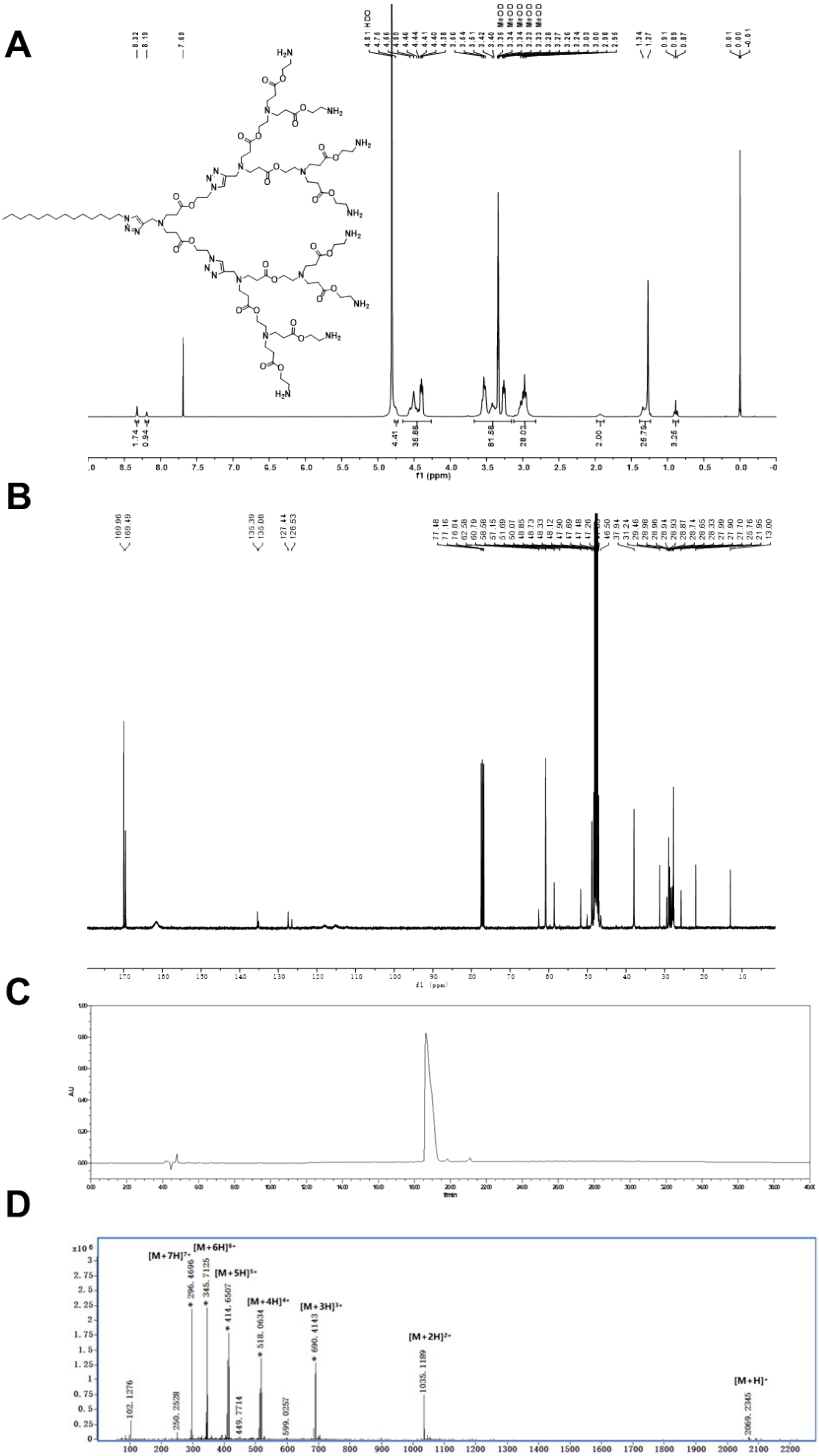


Figure S3 A) ^{1}H NMR, B) ^{13}C NMR, C) HPLC, and D) HRMS spectra of **1b**.

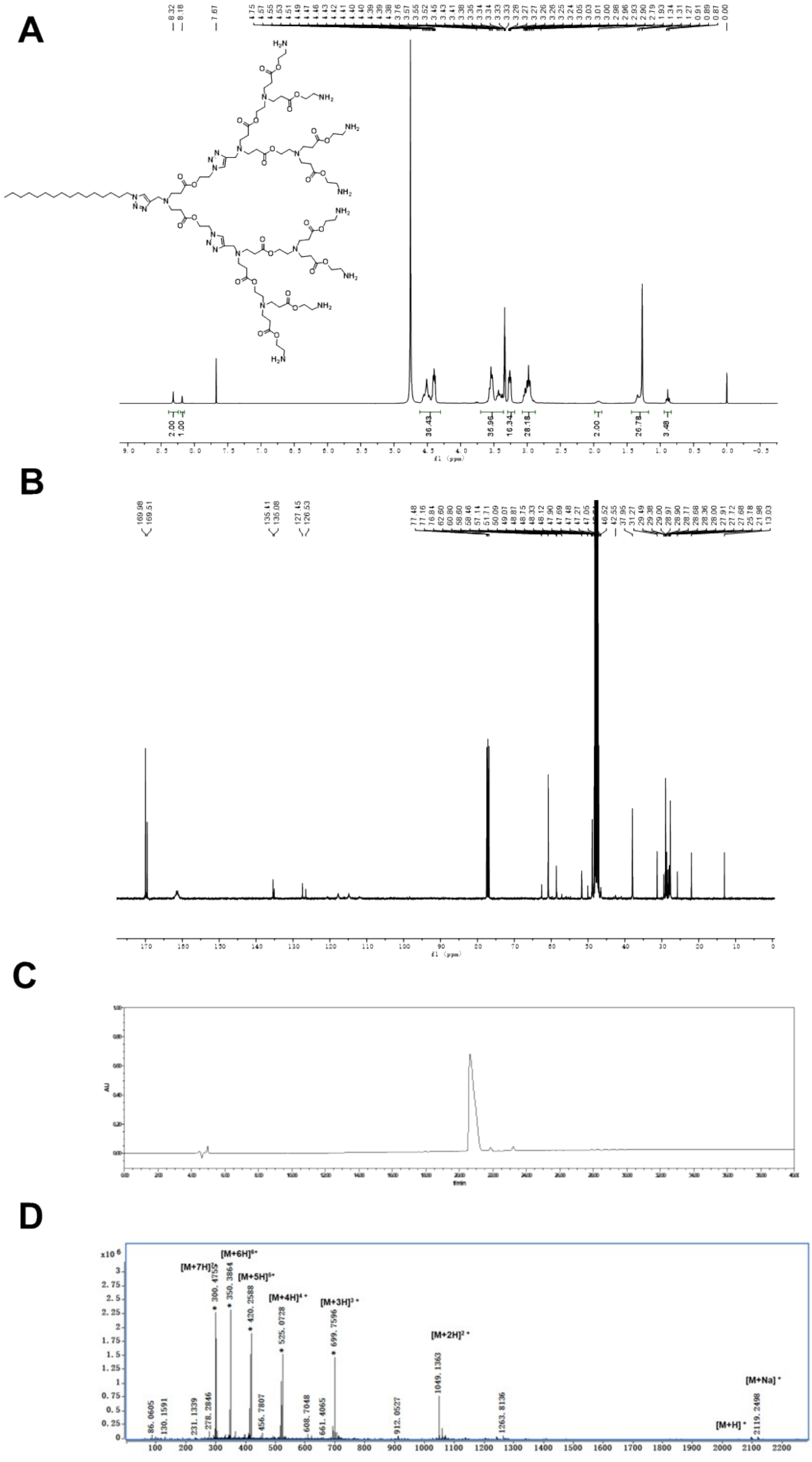


Figure S4 A) ^{1}H NMR, B) ^{13}C NMR, C) HPLC, and D) HRMS spectra of **1c**.

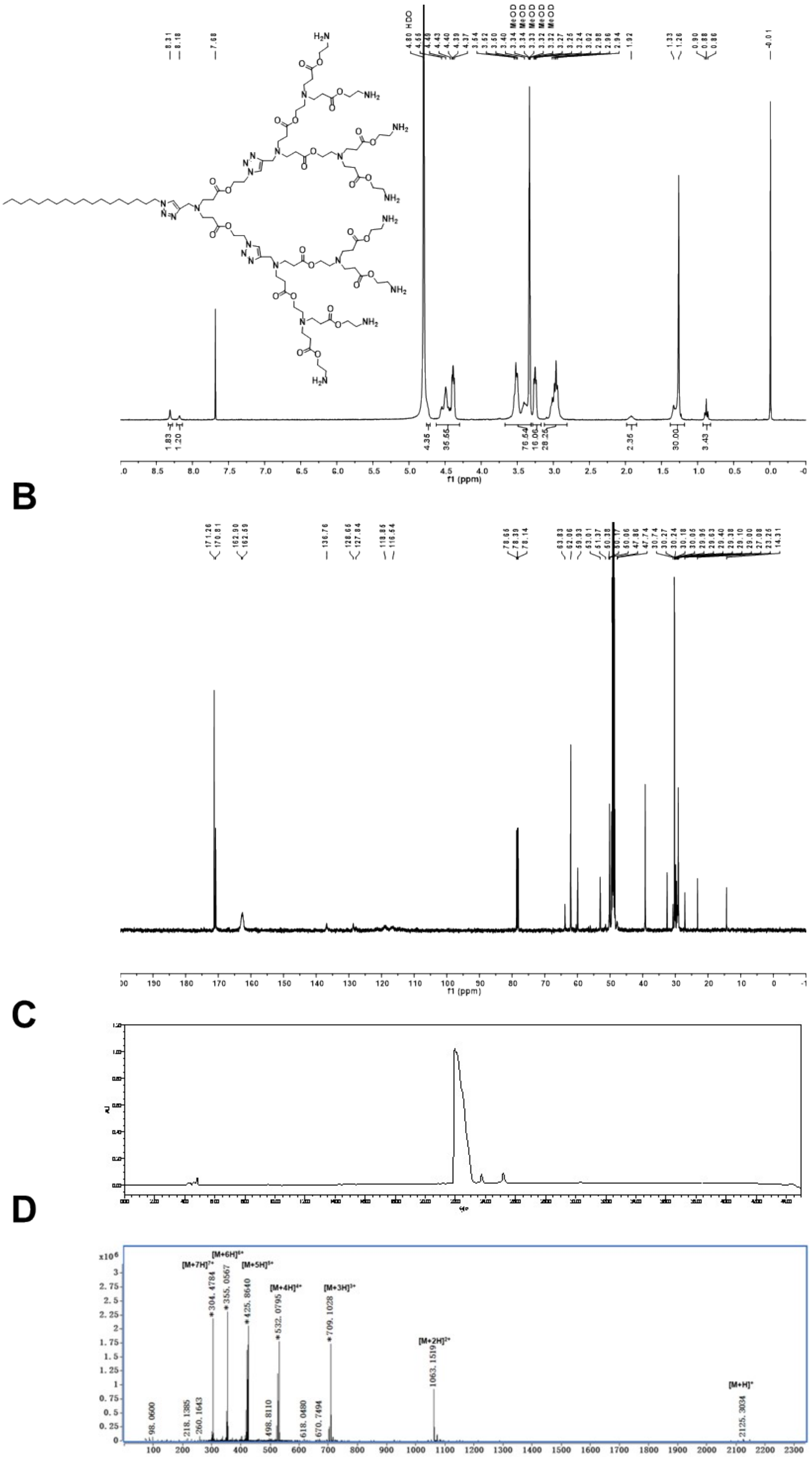


Figure S5 A) ^{1}H NMR, B) ^{13}C NMR, C) HPLC, and D) HRMS spectra of **1d**.

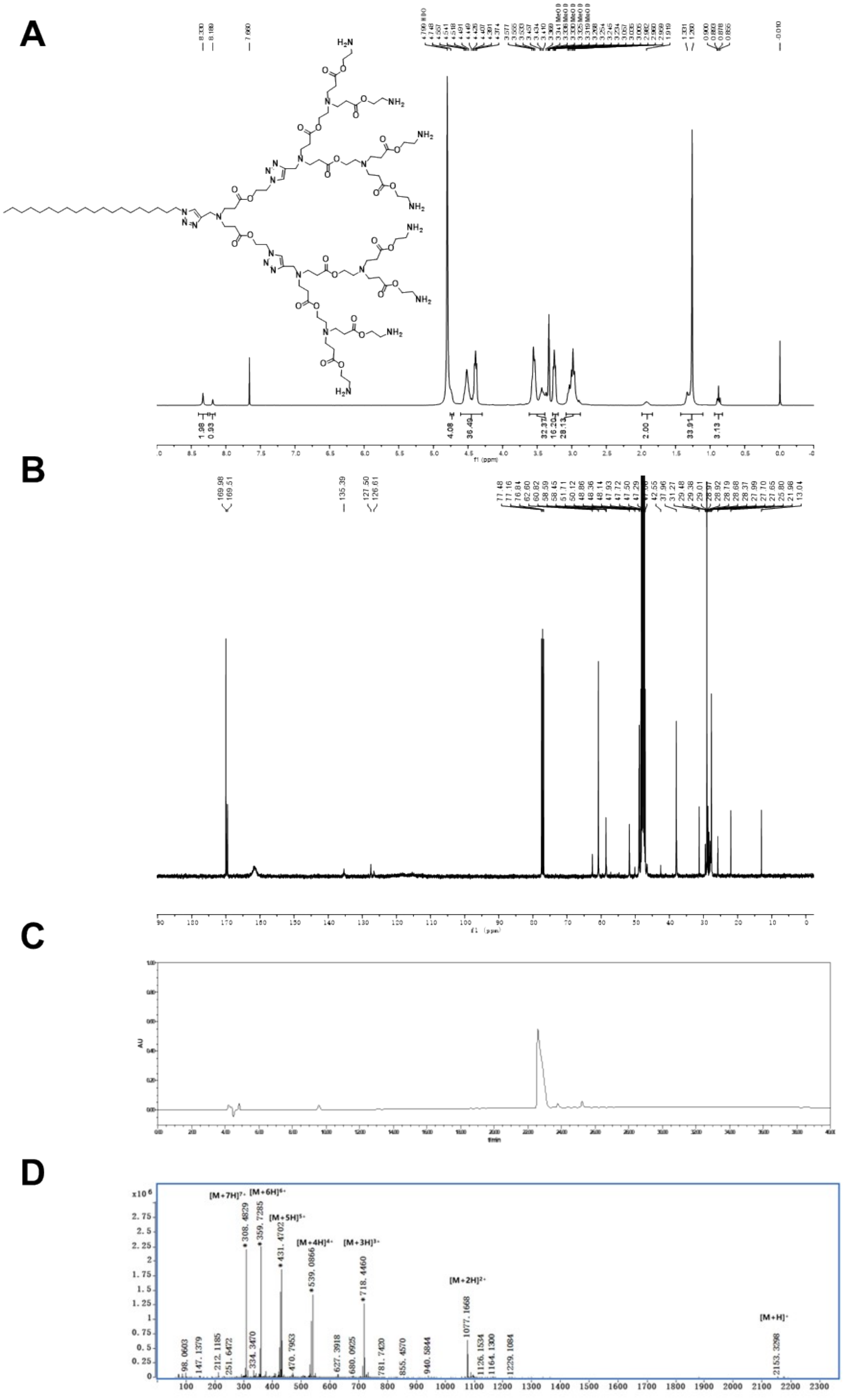


Figure S6 A) ^{1}H NMR, B) ^{13}C NMR, C) HPLC, and D) HRMS spectra of **1e**

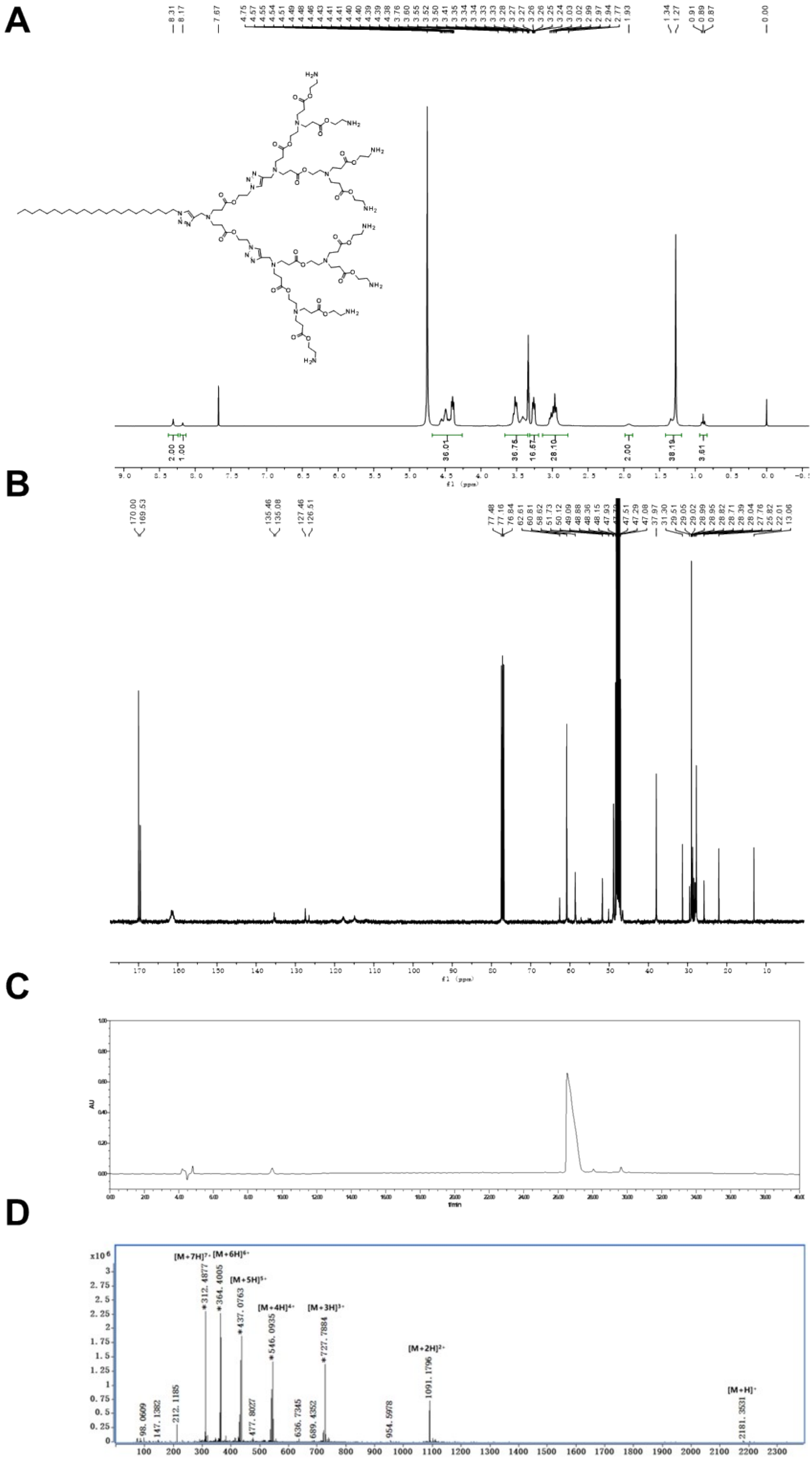
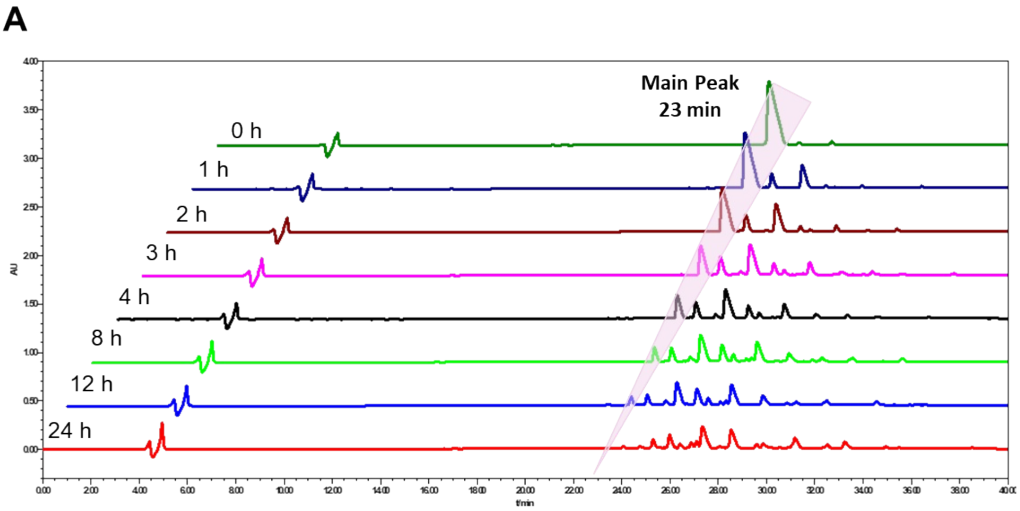


Figure S7 Degradation profiles of PAE dendrimer **1c** in aqueous solution at room temperature monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



B

t (h)	Main Peak Area	Degradation Percentage
0 h	15754656	0
1 h	12558939	20.3
2 h	8196468	48.0
3 h	4112689	73.9
4 h	2737096	82.6
8 h	1256892	92.0
12 h	661958	95.8
24 h	0	100

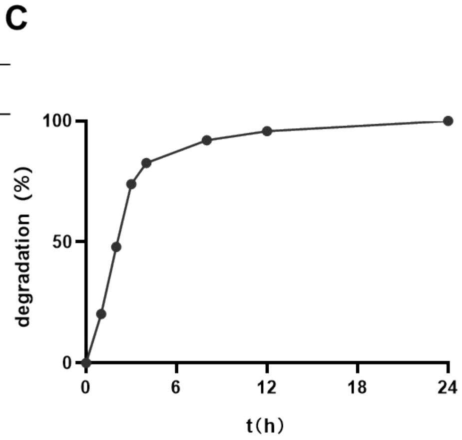
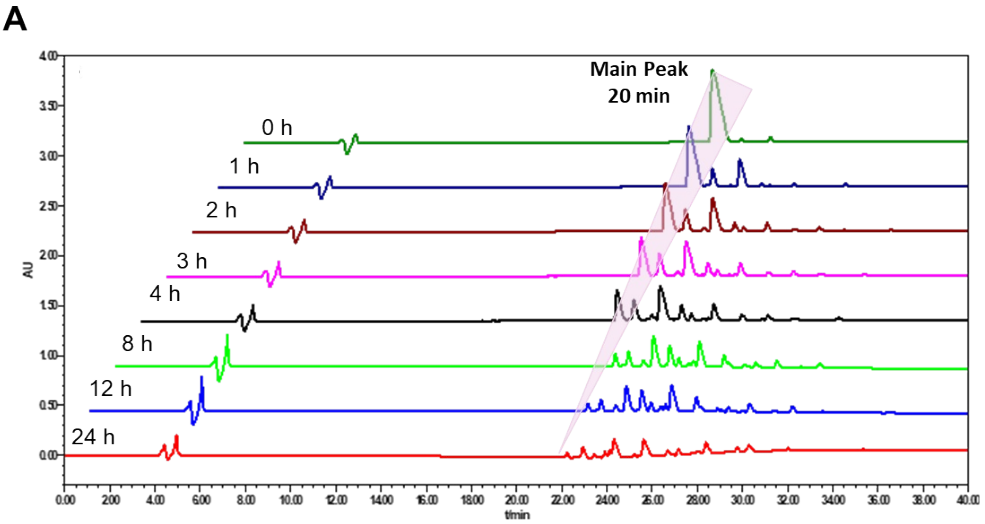


Figure S8 Degradation profiles of PAE dendrimer **1a** in aqueous solution at room temperature monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



B

t (h)	Main Peak Area	Degradation Percentage
0 h	19554303	0
1 h	13168551	32.7
2 h	8858386	54.7
3 h	5895069	69.6
4 h	3983946	79.6
8 h	949606	95.1
12 h	527359	97.3
24 h	0	100

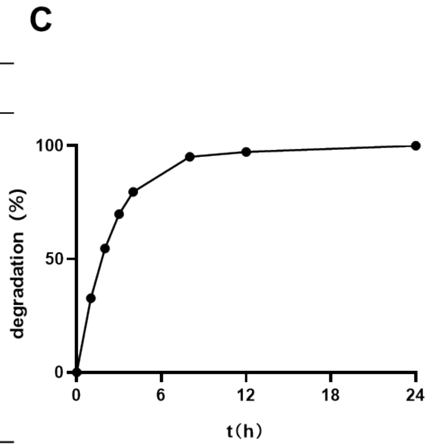
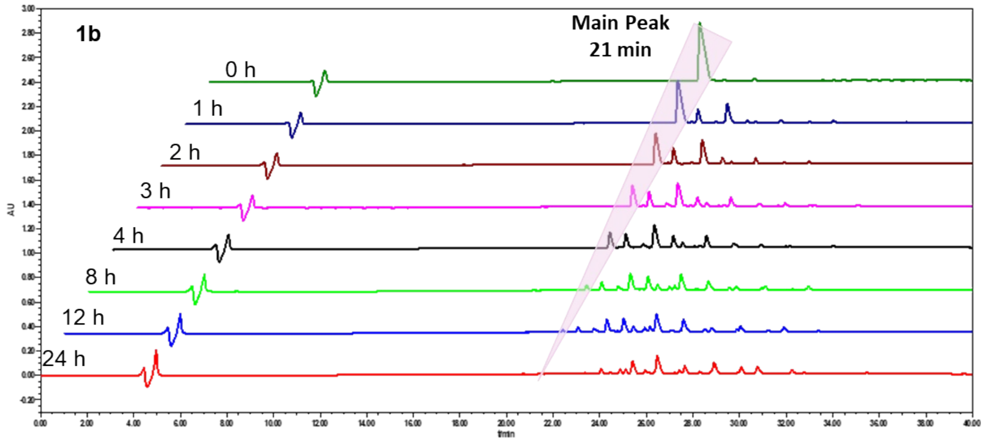


Figure S9 Degradation profiles of PAE dendrimer **1b** in aqueous solution at room temperature monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).

A



B

t (h)	Main Peak Area	Degradation Percentage
0 h	7971808	0
1 h	4577130	42.6
2 h	2780878	65.1
3 h	1636412	79.5
4 h	1059893	86.7
8 h	272559	96.6
12 h	94308	98.8
24 h	0	100

C

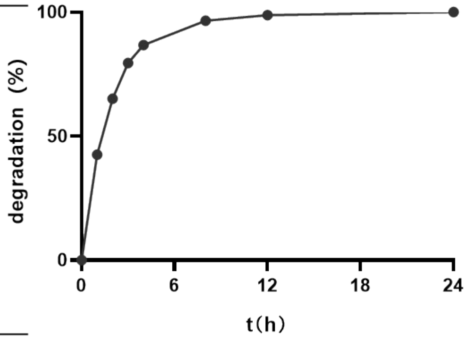
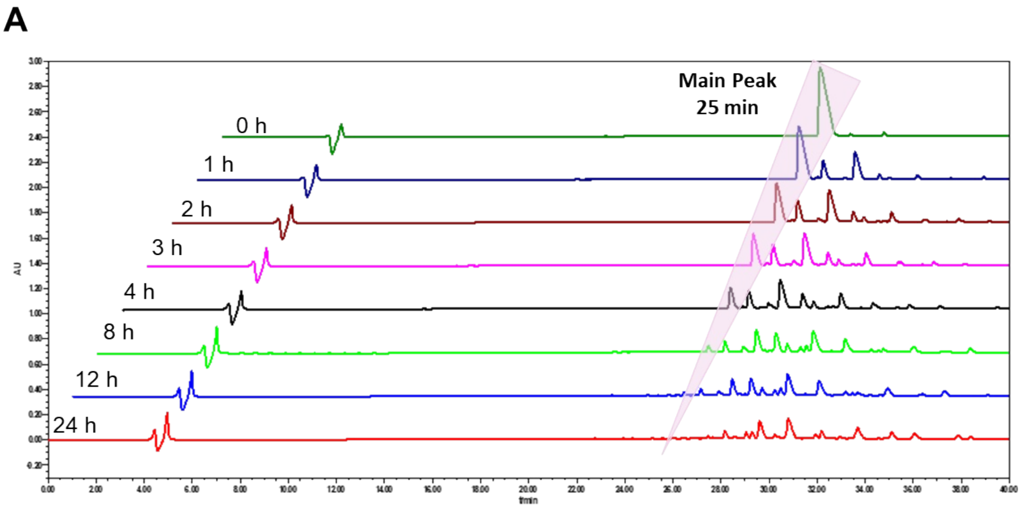


Figure S10 Degradation profiles of PAE dendrimer **1d** in aqueous solution at room temperature monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



B

t (h)	Main Peak Area	Degradation Percentage
0 h	12387022	0
1 h	7780127	37.2
2 h	4471508	63.9
3 h	3041409	75.4
4 h	1664012	86.6
8 h	362330	97.1
12 h	133136	98.9
24 h	0	100

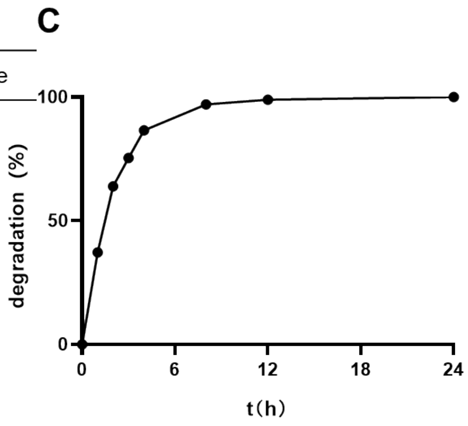
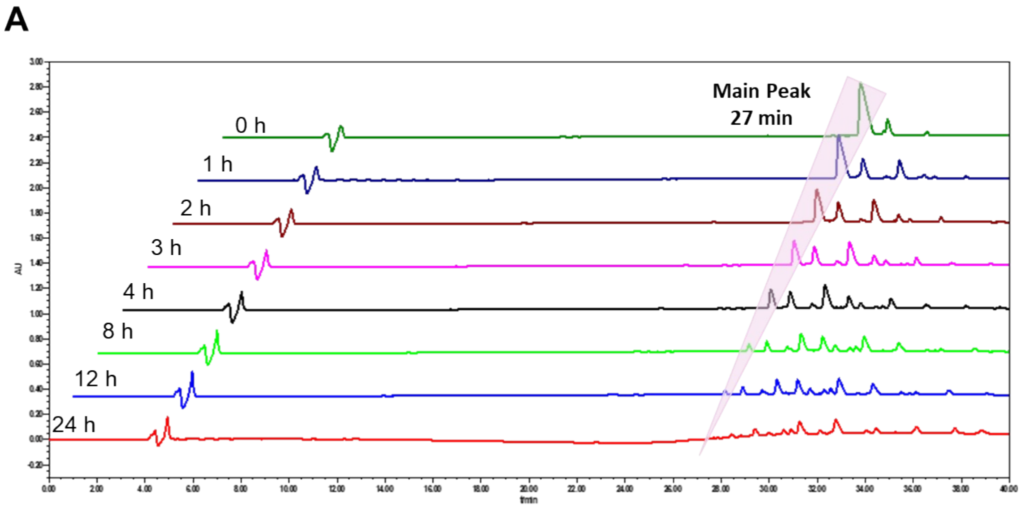


Figure S11 Degradation profiles of PAE dendrimer **1e** in aqueous solution at room temperature monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



B

t (h)	Main Peak Area	Degradation Percentage
0 h	8526055	0
1 h	5721683	32.9
2 h	3713193	56.4
3 h	2417749	71.6
4 h	1552729	81.8
8 h	373742	95.6
12 h	373742	97.9
24 h	0	100

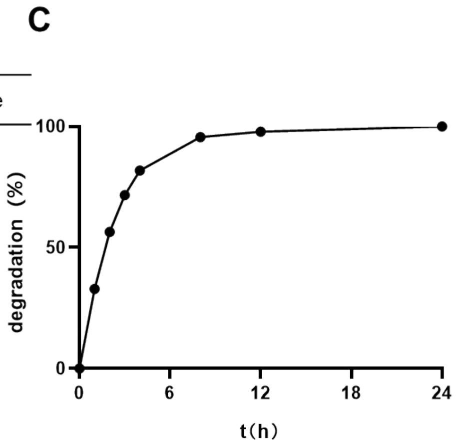
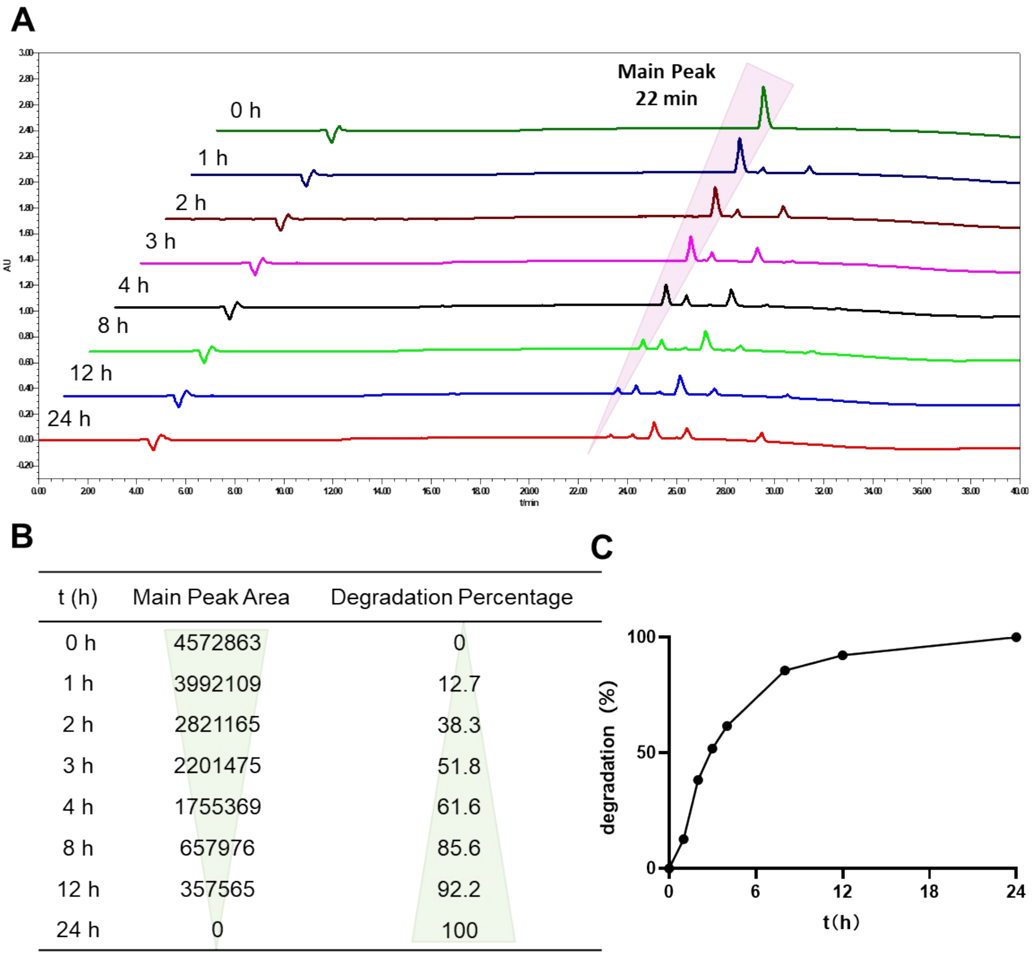
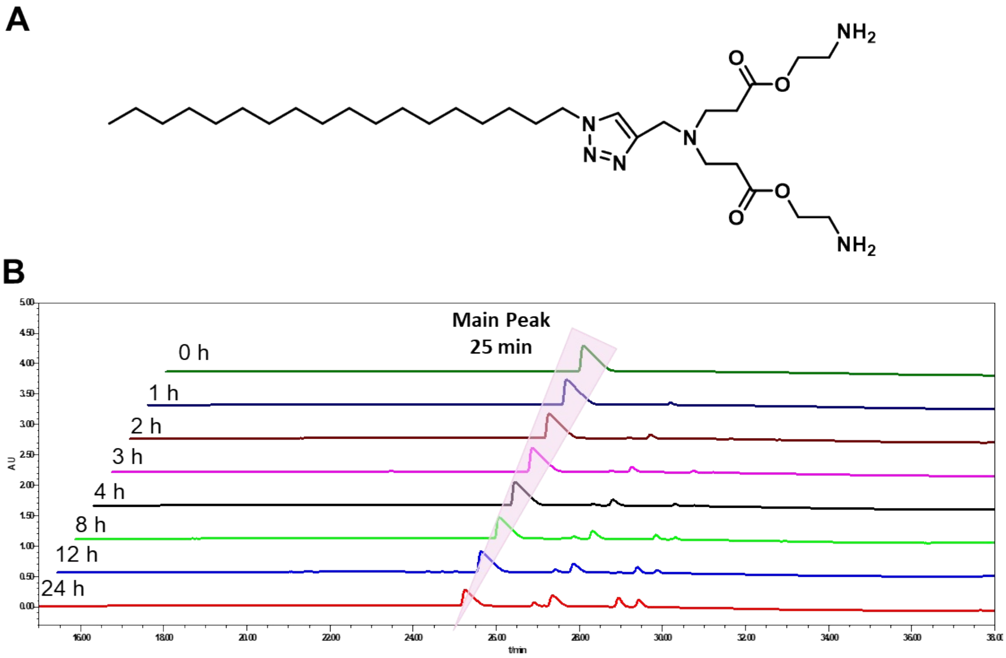


Figure S12 Degradation profiles of PAE dendrimer **I** in aqueous solution at room temperature monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



t (h)	Main Peak Area	Degradation Percentage
0 h	4572863	0
1 h	3992109	12.7
2 h	2821165	38.3
3 h	2201475	51.8
4 h	1755369	61.6
8 h	657976	85.6
12 h	357565	92.2
24 h	0	100

Figure S13 Degradation profiles of PAE dendrimer $\mathbf{I_0}$ in aqueous solution at room temperature monitored by HPLC. A) Chemical structure of $\mathbf{I_0}$; B) Changes in the intensity of the main peak; C) analysis of main peak area and degradation percentage; D) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



C

t (h)	Main Peak Area	Degradation Percentage
0 h	9472359	0
1 h	9326027	1.54
2 h	8987226	5.12
3 h	8449502	10.8
4 h	8033361	15.2
8 h	6963579	26.5
12 h	6627716	31.4
24 h	4390107	53.6

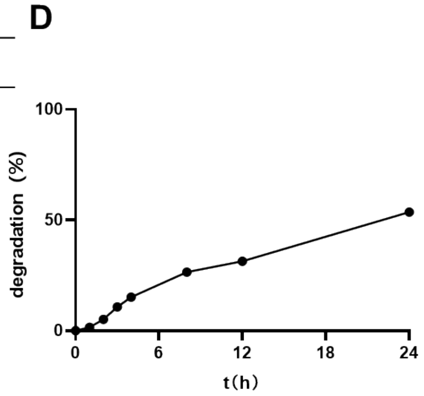


Figure S14 Critical aggregation concentration (CAC) of PAE dendrimers (**1a–1e**) determined using the Nile Red fluorescent probe in pH 7.4 buffer solution at room temperature.

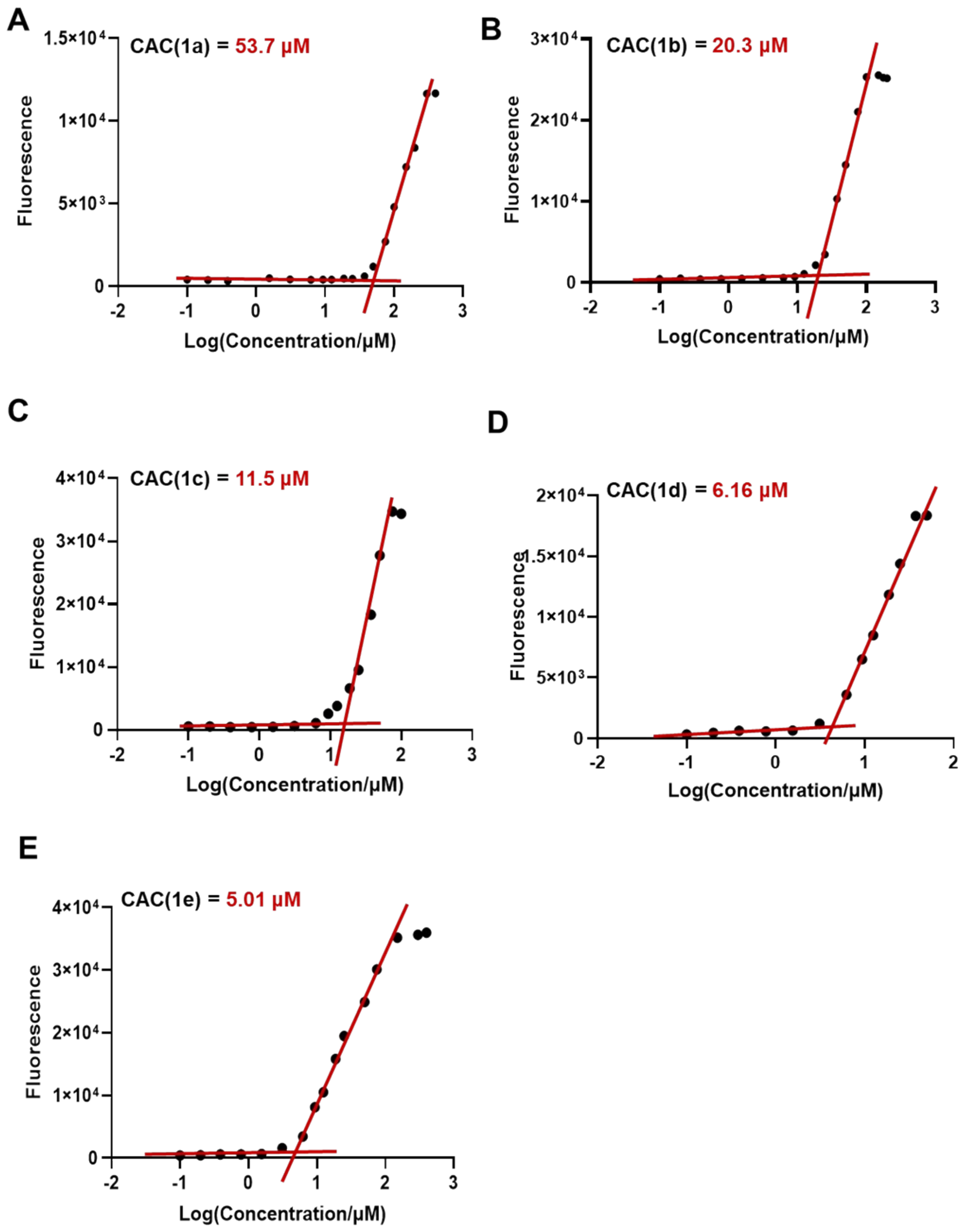


Figure S15 Metabolic toxicity assessment of PAE dendrimers (**1a-1e**) in normal cell lines (L929, L02, MDCK) using the MTT assay following 48 h incubation at 37°C.

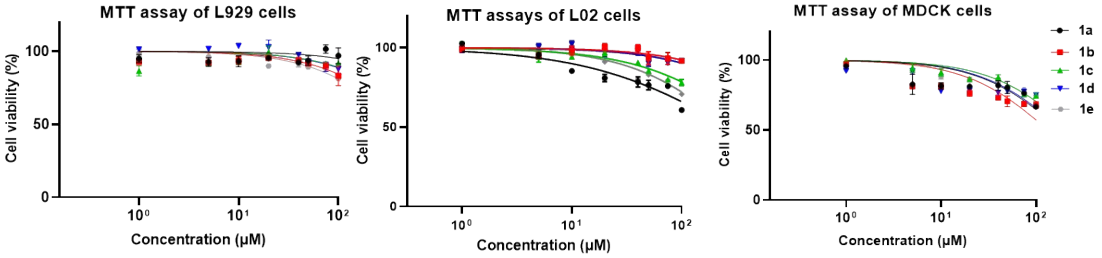
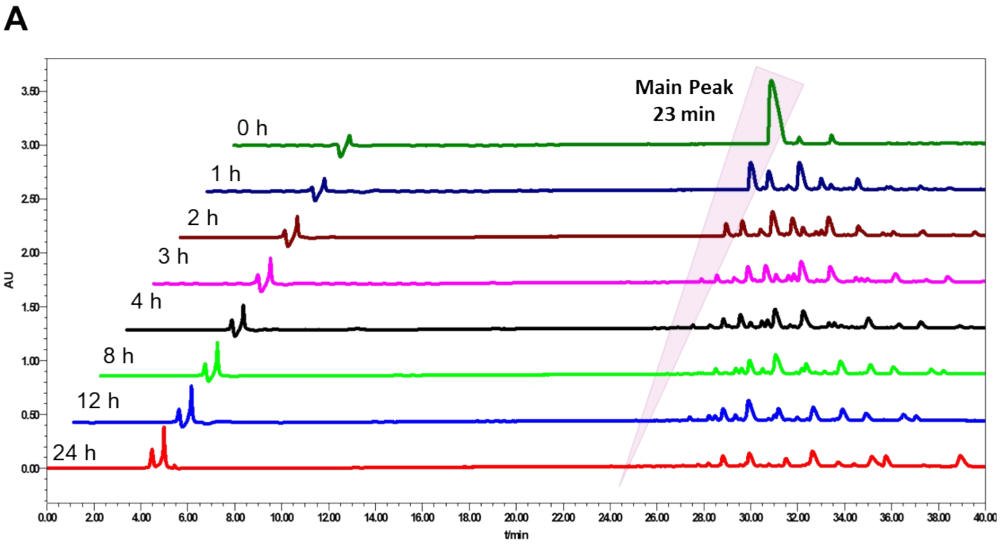
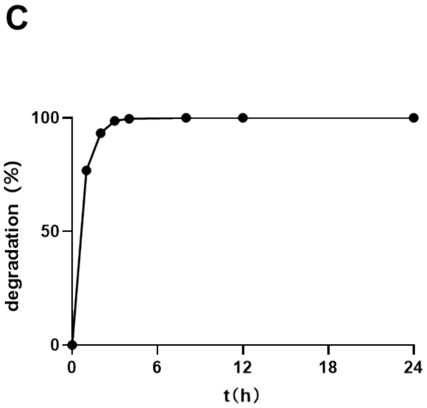


Figure S16 Degradation profiles of PAE dendrimer **1c** in aqueous solution at 37°C monitored by HPLC. A) Changes in the intensity of the main peak; B) analysis of main peak area and degradation percentage; C) degradation curve at different time points (0, 1, 2, 3, 4, 8, 12 and 24 h).



B

t (h)	Main Peak Area	Degradation Percentage
0 h	14518805	0
1 h	3353373	76.9
2 h	966621	93.3
3 h	190340	98.7
4 h	56149	99.6
8 h	0	100
12 h	0	100
24 h	0	100



General experimental information

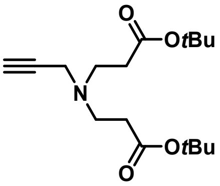
Propargylamine, tert-butyl acrylate, monoethanolamine, 1-nonanol, malonic acid, p-Toluenesulfonic acid (TsOH), 7-Bromo-1-heptanol, tosyl chloride (TsCl), trifluoroacetic acid (TFA), chloroacetonitrile ($ClCH_2CN$), 4-Dimethylaminopyridine (DMAP), benzoic anhydride (Bz_2O), Di-tert-butyl decarbonate (Boc_2O), cesium fluoride (CsF), azidotrimethylsilane (TMSA), and sodium ascorbate were purchased from Aladdin Biochemical Technology Co., Ltd. (Shanghai, China). Toluene, copper(II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$), and triethylamine (Et_3N) were obtained from Nanjing Chemical Reagent Co., Ltd. (Jiangsu, China). 1,8-Diazabicyclo [5.4.0] undec-7-ene (DBU) was purchased from Energy Chemical Ltd. (Shanghai, China). Petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM), methanol (CH_3OH), ethanol (EtOH), acetonitrile (CH_3CN) and N, N-Dimethylformamide (DMF) were distilled prior to use.

All reactions were conducted under strictly anhydrous and inert conditions (nitrogen or argon atmosphere) at temperatures ranging from 25°C to 50°C, including room temperature, as specified. Solvents and reagents were dried using standard protocols before use. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F254 aluminum-backed plates (200 μm thickness). Product spots were visualized by iodine staining and/or phosphomolybdic acid solution. Products were purified by flash column chromatography using Macherey-Nagel silica gel 200 M (particle size 40–63 μm). Purity of compounds was analyzed by HPLC using a Waters 1525 pump equipped with a 2998 photodiode array detector (PDA). NMR spectra were recorded at room temperature on Bruker Avance-300, Bruker Avance-400 and Bruker Avance-50 spectrometers. MS were obtained on an Agilent 6230 instrument.

Synthesis and characterization

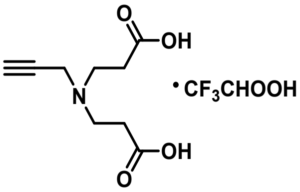
PAE hydrophilic dendrons (**4** and **13**) and azido-bearing alkyl chain (**10a-e**) were synthesized following previously reported procedures.[1-3]

Synthesis and characterization of alkynyl-containing PAE dendrons



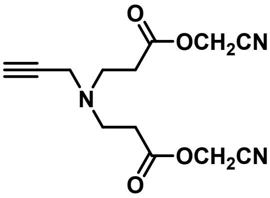
2

2: To a solution of propargylamine (220.0 mg, 4.0 mmol) in anhydrous methanol (5.4 mL) at 0 °C under nitrogen was added *tert*-butyl acrylate (1843.2 mg, 14.4 mmol) dropwise. The reaction mixture was stirred at 30°C for 72 h in the dark. Volatiles were removed under reduced pressure to yield a yellowish crude oil. Purification by flash column chromatography (silica gel, PE/EA = 15:1 to 5:1) afforded compound **2** as a colorless oil (906.0 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.43 (d, *J* = 2.4 Hz, 2H), 2.81 (t, *J* = 7.3 Hz, 4H), 2.39 (t, *J* = 7.6 Hz, 4H), 2.21 (t, *J* = 2.4 Hz, 1H), 1.46 (s, 18H).



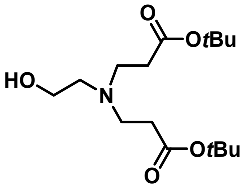
3

3: Compound **2** (1000.0 mg, 3.22 mmol) was dissolved in DCM (50.0 mL) under nitrogen, and TFA (4.8 mL, 64.4 mmol) was added dropwise at 0°C. The reaction mixture was stirred at 30°C for 48 h in the dark. After removal of solvents under reduced pressure, the residue was washed with anhydrous Et_2O (150 mL × 3) to afford compound **3** as a white solid (876.8 mg, 87%). ^{1}H NMR (300 MHz, CD_3OD): δ 4.23 (d, *J* = 2.6 Hz, 2H), 3.56 (t, *J* = 6.7 Hz, 4H), 3.40 (t, *J* = 2.5 Hz, 1H), 2.89 (t, *J* = 6.7 Hz, 4H).



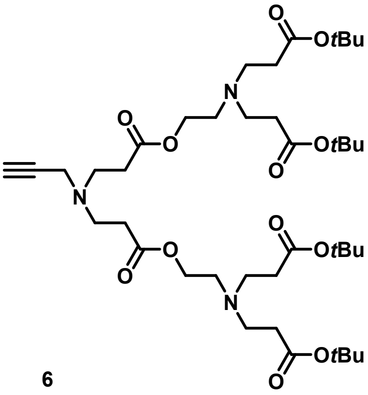
4

4: To a solution of compound **3** (270.0 mg, 0.862 mmol) in DMF under nitrogen at 0°C was added NEt_3 (0.72 mL, 5.18 mmol), followed by chloroacetonitrile (0.44 mL, 6.91 mmol). The reaction mixture was stirred at 30°C for 24 h in the dark. After evaporation of the solvent, the residue was then diluted with water (20.0 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (PE/EA = 3/1) afforded compound **4** as a colorless oil (203.0 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.74 (s, 4H), 3.43 (d, *J* = 2.4 Hz, 2H), 2.88 (t, *J* = 6.6 Hz, 4H), 2.56 (t, *J* = 6.6 Hz, 4H), 2.23 (t, *J* = 2.4 Hz, 1H).



5

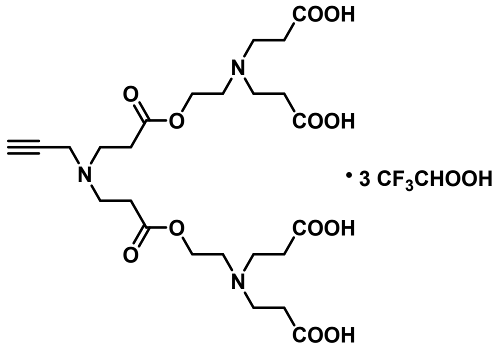
5: Ethanolamine (220.0 mg, 3.6 mmol) was dissolved in CH_3OH (5.0 mL) under nitrogen, and *tert*-butyl acrylate (1.9 mL, 13.0 mmol) was added dropwise at 0°C. The reaction mixture was stirred at 30°C for 48 h in the dark. After removal of solvents under reduced pressure, the crude product was purified by silica gel column chromatography (PE/EA = 2/1) to afford compound **5** as a colorless oil (1051.0 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.58 (t, *J* = 5.0 Hz, 2H), 2.77 (t, *J* = 6.9 Hz, 4H), 2.59 (t, *J* = 4.5 Hz, 2H), 2.37 (t, *J* = 6.9 Hz, 4H), 1.45 (s, 18H).



6

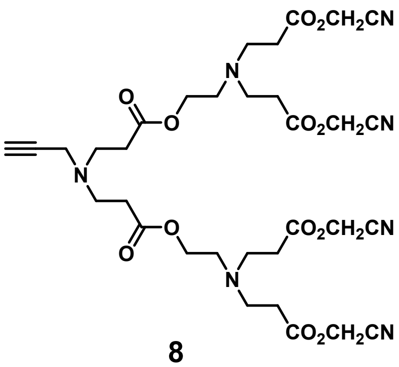
6: Compound **5** (500.0 mg, 1.59 mmol) was dissolved in CH_3CN (1.5 mL) under nitrogen. To this solution at 0°C was added DBU (0.24 mL, 1.59 mmol), followed by a solution of **4** (100.0 mg, 0.36 mmol) in CH_3CN (3.0 mL) dropwise. The reaction mixture was stirred at 30°C for 10 h in the dark. After solvent removal under reduced pressure, the residue was diluted with water (20 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with saturated NaCl (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated to afford the crude product.

The crude product was then treated with benzoic anhydride (623.76 mg, 2.76 mmol) and DMAP (674.6 mg, 5.53 mmol) in DCM (10.0 mL). The mixture was stirred at 30°C for 2 h in the dark. After removal of solvents under reduced pressure, the reaction mixture was washed sequentially with saturated $NaHCO_3$ solution (30 mL × 3) and saturated NaCl solution (30 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel column chromatography (PE/EA = 2/1) afforded compound **6** as a colorless oil (201.0 mg, 70%). ^1H NMR (300 MHz, $CDCl_3$): δ 4.13 (t, *J* = 6.3 Hz, 4H), 3.43 (d, *J* = 2.4 Hz, 2H), 2.83 (dt, *J* = 14.7, 7.3 Hz, 12H), 2.72 (t, *J* = 6.3 Hz, 4H), 2.49 (t, *J* = 7.2 Hz, 4H), 2.37 (t, *J* = 7.3 Hz, 8H), 2.26 – 2.17 (m, 1H), 1.46 (s, 36H).



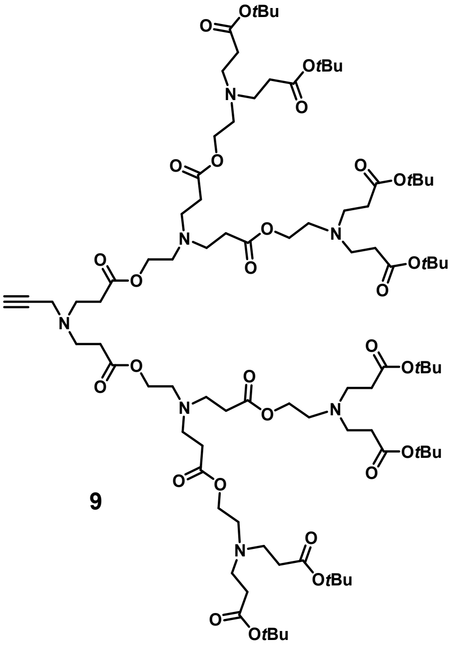
7

7: Compound **6** (2000.0 mg, 2.5 mmol) was dissolved in DCM (20.0 mL) under nitrogen, and TFA (7.6 mL, 100 mmol) was added dropwise at 0°C. The reaction mixture was stirred at 30°C for 48 h in the dark. After removal of solvents under reduced pressure, the residue was washed with anhydrous Et_2O (200 mL × 3) to afford compound **7** as a white solid (2110.0 mg, 93%). ^1H NMR (300 MHz, CD_3OD): δ 4.57 (t, *J* = 4.9 Hz, 4H), 4.14 (d, *J* = 2.5 Hz, 2H), 3.70 – 3.44 (m, 16H), 3.27 (t, *J* = 3 Hz, 1H), 2.92 (m, 12H).



8

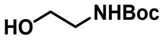
8: To a solution of Compound **7** (205.0 mg, 0.22 mmol) in DMF (4.0 mL) under nitrogen at 0°C was added NEt_3 (0.38 mL, 2.69 mmol), followed by $ClCH_2CN$ (0.24 mL, 3.58 mmol). The reaction mixture was stirred at 30°C for 32 h in the dark. After removal of solvent under reduced pressure, the residue was diluted with water (30 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (PE/EA = 1/1 to 1/3) afforded compound **8** as a colorless oil (123.0 mg, 77%). ^1H NMR (300 MHz, DMSO): ^1H NMR (300 MHz, DMSO-d6) δ 4.94 (s, 8H), 4.01 (t, J = 6.0 Hz, 4H), 3.17 – 3.08 (m, 1H), 2.83 – 2.60 (m, 16H), 2.55 (d, J = 6.6 Hz, 18H), 2.41 (t, J = 7.0 Hz, 4H).



9

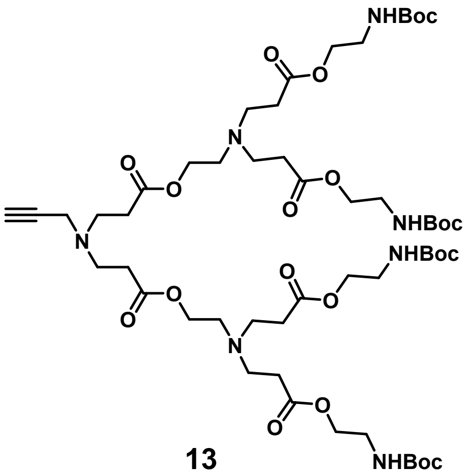
9: Compound **5** (133.3 mg, 0.42 mmol) was dissolved in MeCN (1.0 mL) under nitrogen at 0°C. To this solution was added DBU (0.026 mL, 0.42 mmol), followed by a solution of compound **8** (35 mg, 0.048 mmol) in CH_3CN (1.0 mL) dropwise. The reaction mixture was stirred at 30°C for 10 h in the dark. After removal of solvent under reduced pressure, the residue was diluted with water (20 mL) and extracted with EtOAc (20 mL×3). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford crude product.

The crude product was then treated with benzoic anhydride (167.2 mg, 0.74 mmol) and DMAP (179.3 mg, 1.47 mmol) in DCM (10 mL). The mixture was stirred at 30°C for 2 h in the dark. After removal of solvents under reduced pressure, the reaction mixture was washed sequentially with saturated $NaHCO_3$ solution (30 mL × 3) and saturated NaCl solution (30 mL), dried over Na_2SO_4, filtered, and concentrated. Purification by silica gel column chromatography (PE/EA = 1/2 to 1/4) afforded compound **9** (15.3 mg, 18%).^{1}H NMR (300 MHz, $CDCl_3$) δ 4.11 (t, *J* = 6.2 Hz, 12H), 3.41 (d, *J* = 2.0 Hz, 2H), 2.98 – 2.58 (m, 40H), 2.53 – 2.28 (m, 28H), 2.22 (t, *J* = 2.1 Hz, 1H), 1.44 (s, 72H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.32, 172.18, 171.86, 80.48, 78.18, 73.61, 62.69, 62.49, 52.14, 52.05, 50.07, 49.72, 49.03, 41.94, 34.08, 33.01, 32.74, 28.22.



15

15: Ethanolamine (2000.0 mg, 330 mmol) was dissolved in CH_3OH (80 mL) under nitrogen at 0°C. Boc_2O (13 mL, 56 mmol) was added, and the reaction mixture was stirred at 30°C for 3 h. After removal of solvents and reagents under reduced pressure, the crude product was purified by silica gel column chromatography (PE/EA= 2/1) to afford compound **15** as a colorless oil (4730.0 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.55 (t, *J* = 5.9 Hz, 2H), 3.15 (t, *J* = 5.9 Hz, 2H), 1.44 (s, 9H).

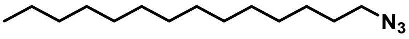


13

13: Compound **15** (260.0 mg, 1.6 mmol) was dissolved in CH_3CN (9.0 mL) under nitrogen at 0°C. To this solution was added DBU (0.24 mL, 1.6 mmol), followed by compound **8** (250.0 mg, 0.34 mmol) dropwise. The reaction mixture was stirred at 30°C for 10 h in the dark. After removal of solvent under reduced pressure, the residue was diluted with water (30 mL) and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by silica gel column chromatography (DCM/EtOH = 40/1 to 25/1) afforded compound **13** as a colorless oil (253.3 mg, 65%). ^1H NMR (300 MHz, $CDCl_3$): 4.22 – 4.07 (m, 12H), 3.48 – 3.30 (m, 10H), 2.84 (t, *J* = 7.0 Hz, 12H), 2.73 (t, *J* = 6.1 Hz, 4H), 2.47 (t, *J* = 7.0 Hz, 12H), 2.21 (t, *J* = 2.2 Hz, 1H), 1.44 (s, 36H).

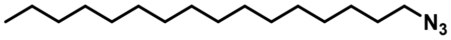
Synthesis and characterization of azido-bearing alkyl chains (C_{14} to C_{22})

To a solution of compound of **16** (0.6 mmol, 1.0 equiv.) and CsF (0.9 mmol, 1.5 equiv.) in DMF (2.0 mL) under nitrogen at 0°C was added TMSA (0.9 mmol, 1.5 equiv.) dropwise. The reaction mixture was stirred at 50°C for 12 h in the dark. After removal of the solvent under reduced pressure, a yellowish crude oil product was obtained. The crude residue was diluted with water (30 mL) and extracted with DCM (30 mL × 3). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (PE) afford compound **10a-e** as colorless oils.



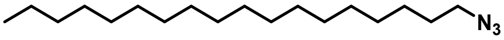
10a

10a: Colorless oil; Yield: 136.5 mg (95%); prepared according to general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.25 (t, *J* = 7.0 Hz, 2H), 1.67 – 1.52 (m, 2H), 1.42 – 1.16 (m, 22H), 0.88 (t, *J* = 6.7 Hz, 3H); IR (cm^{-1}): υ 2093.34 (-N$_3$).



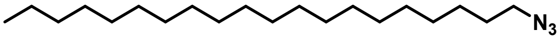
10b

10b: Colorless oil; Yield: 152.5 mg (95%); prepared according to general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.25 (t, *J* = 7.0 Hz, 2H), 1.67 – 1.52 (m, 2H), 1.42 – 1.16 (m, 26H), 0.88 (t, *J* = 6.7 Hz, 3H); IR (cm^{-1}): *υ* 2092.80 (-N$_3$).



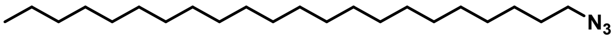
10c

10c: Colorless oil; Yield: 164.9 mg (93%); prepared according to general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.25 (t, *J* = 7.0 Hz, 2H), 1.68 – 1.50 (m, 2H), 1.44 – 1.11 (m, 30H), 0.88 (t, *J* = 6.0 Hz, 3H); IR (cm^{-1}): *υ* 2091.81 (-N$_3$).



10d

10d: Colorless oil; Yield: 182.5 mg (94%); prepared according to general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.25 (t, *J* = 7.0 Hz, 2H), 1.68 – 1.51 (m, 2H), 1.45 – 1.15 (m, 34H), 0.88 (t, *J* = 6.0 Hz, 3H); IR (cm^{-1}): *υ* 2093.87 (-N$_3$).

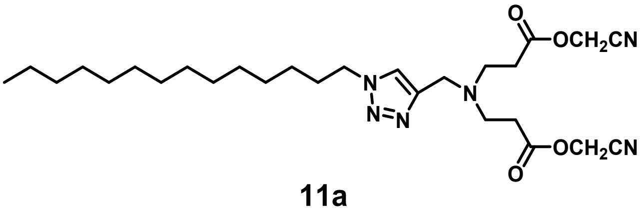


10e

10e: Colorless oil; Yield: 202.5 mg (96%); prepared according to general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.25 (t, *J* = 7.0 Hz, 2H), 1.70 – 1.50 (m, 2H), 1.43 – 1.16 (m, 38H), 0.88 (t, *J* = 7.5 Hz, 3H); IR (cm^{-1}): *υ* 2094.30 (-N$_3$).

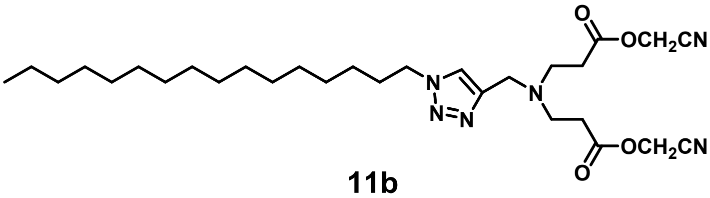
Synthesis and characterization of (11a-11e)

To a solution of compound **10** (0.2 mmol, 1.0 equiv.), CuSO$_4$·5H$_2$O (0.01 mmol, 0.1 equiv.), and sodium ascorbate (0.2 mmol, 1.0 equiv.) in DMF (4.0 mL) under nitrogen at 0°C was added compound **4** (0.21 mmol, 1.1 equiv.) dropwise. The reaction mixture was stirred at 30°C for 3 h in the dark. After removal of the solvent under reduced pressure, the crude residue was diluted with DCM (30 mL), and washed with saturated NH_4Cl solution (30 mL × 3) and saturated NaCl solution (30 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (PE/EA= 2/1 to 1/3) afforded compound **11a-11e** as colorless oils.



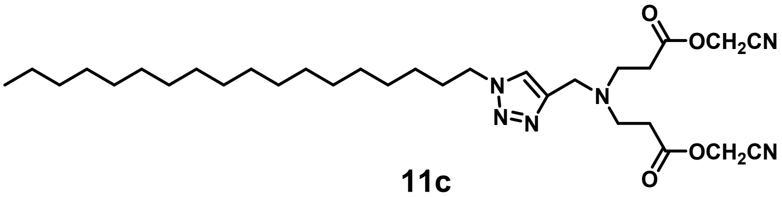
11a

11a: Colorless oil; yield: 82.1 mg (81%), prepared according to the general procedure; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (s, 1H), 4.72 (s, 4H), 4.34 (t, *J* = 7.2 Hz, 2H), 3.78 (s, 2H), 2.84 (t, *J* = 3 Hz, 4H), 2.59 (s, 4H), 1.90 (t, *J* = 6 Hz, 2H)， 1.39 – 1.16 (m, 22H), 1.44 – 1.11 (m, 30H), 0.87 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ170.81, 144.07, 114.70, 48.89, 48.53, 48.37, 32.34, 31.91, 30.27, 29.67, 29.65, 29.64, 29.61, 29.53, 29.41, 29.35, 29.00, 26.48, 22.68, 14.14.



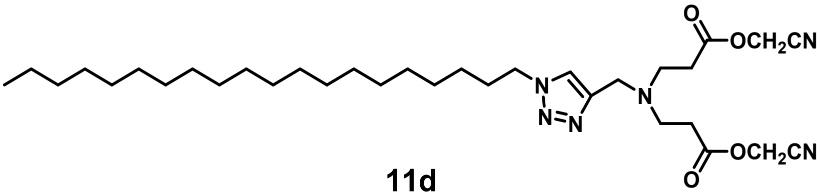
11b

11b: Colorless oil; yield: 87.2 mg (80%), prepared according to the general procedure; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (s, 1H), 4.72 (s, 4H), 4.34 (t, *J* = 7.5 Hz, 2H), 3.79 (s, 2H), 2.84 (t, *J* = 5.9 Hz, 4H), 2.59(t, *J* = 6.3 Hz, 4H), 1.90 (t, *J* = 6 Hz, 2H)， 1.41 – 1.17 (m, 26H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.82, 122.73, 114.70, 50.40, 48.91, 48.55, 48.37, 32.37, 31.92, 30.28, 29.69, 29.66, 29.63, 29.54, 29.42, 29.36, 29.02, 26.49, 22.70, 14.15.



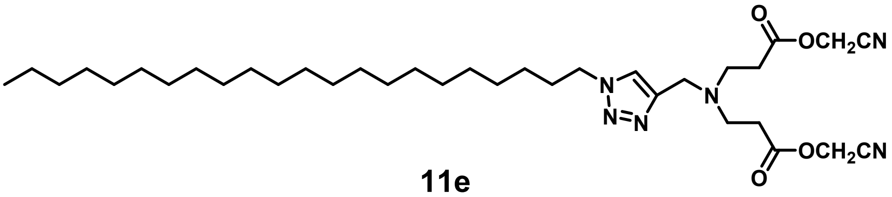
11c

11c: Colorless oil; yield: 106.5 mg (93%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (s, 1H), 4.72 (s, 4H), 4.33 (t, *J* = 7.3 Hz, 2H), 3.79 (s, 2H), 2.83 (t, *J* = 5.6 Hz, 4H), 2.59 (t, *J* = 5.7 Hz, 4H), 2.01 – 1.78 (m, 2H), 1.44 – 1.12 (m, 30H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.89, 144.26, 122.76, 114.71, 50.51, 49.04, 48.71, 48.43, 32.49, 32.04, 30.40, 29.81, 29.78, 29.74, 29.66, 29.54, 29.48, 29.13, 26.61, 22.81, 14.25.



11d

11d: Colorless oil; yield: 106.5 mg (93%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (s, 1H), 4.72 (s, 4H), 4.33 (t, *J* = 7.3 Hz, 2H), 3.79 (s, 2H), 2.83 (t, *J* = 6.5 Hz, 4H), 2.59(t, *J* = 6.5 Hz, 4H)， 1.90 (t, *J* = 6 Hz, 2H)， 1.45 - 1.10 (m, 34H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.81, 144.12, 122.73, 114.69, 50.41, 48.97, 48.60, 48.38, 32.41, 31.95, 30.31, 29.73, 29.66, 29.57, 29.45, 29.39, 29.04, 26.53, 22.72, 14.16.

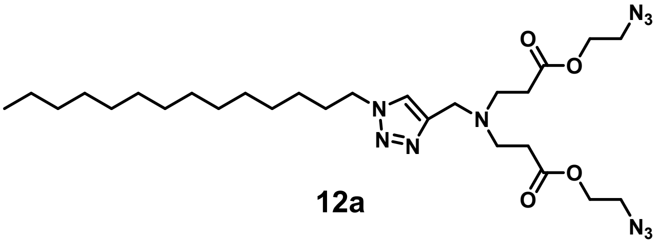


11e

11e: Colorless oil; yield: 106.5 mg (93%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ7.48 (s, 1H), 4.72 (s, 4H), 4.33 (t, *J* = 7.5 Hz, 2H), 3.79 (s, 2H), 2.83 (t, *J* = 6.5 Hz, 4H), 2.59(t, *J* = 6.0 Hz, 4H), 1.90 (t, *J* = 6 Hz, 2H), 1.39 - 1.18 (m, 38H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.85, 144.17, 122.73, 114.71, 50.44, 48.98, 48.63, 48.40, 32.43, 31.98, 30.34, 29.76, 29.71, 29.69, 29.60, 29.48, 29.42, 29.07, 26.55, 22.75, 14.19.

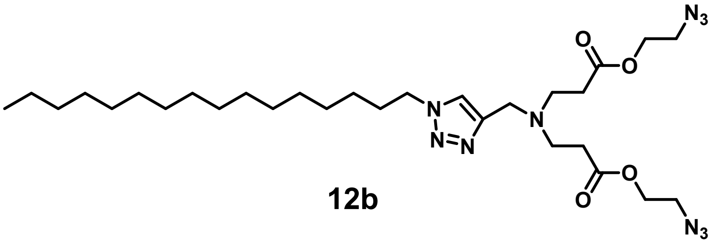
Synthesis and characterization of 12

To a solution of 2-Azidoethanol (0.93 mmol, 4.4 equiv.) in CH_3CN (1.0 mL) under nitrogen at 0°C was added DBU (0.93 mmol, 4.4 equiv.) followed by a solution of dendron **11** (0.21 mmol, 1.0 equiv.) in CH_3CN (2.0 mL) dropwise. The reaction mixture was stirred at 30°C for 24 h. After removal of the solvent under reduced pressure, the crude product was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (PE/EA= 1/1 to 1/2) afforded **12** as a colorless oil.



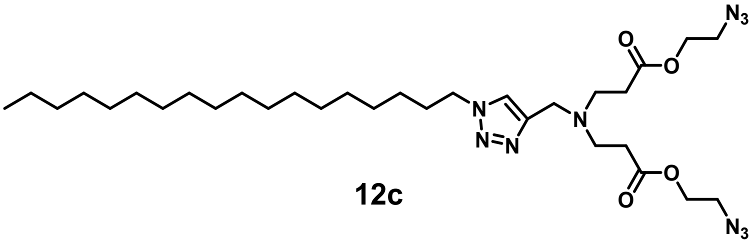
12a

12a: Colorless oil; yield: 89.6 mg (74%), prepared according to the general procedure; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46 (s, 1H), 4.32 (t, *J* = 6.0 Hz, 2H), 4.24 (t, *J* = 6.0 Hz, 4H), 3.83 (s, 1H), 3.48 (t, *J* = 6.0 Hz, 2H), 2.84 (t, *J* = 6.0 Hz, 4H), 2.57 (t, *J* = 7.5 Hz, 4H), 1.89 (t, *J* = 6.0 Hz, 4H), 1.36 – 1.20 (m, 22H), 0.87 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.06, 144.25, 122.42, 62.98, 50.35, 49.74, 48.83, 48.43, 32.66, 31.94, 30.34, 29.70, 29.67, 29.63, 29.56, 29.43, 29.38, 29.04, 26.53, 22.72, 14.17. IR (cm^{-1}): *υ* 2093.34 ($-N_3$).



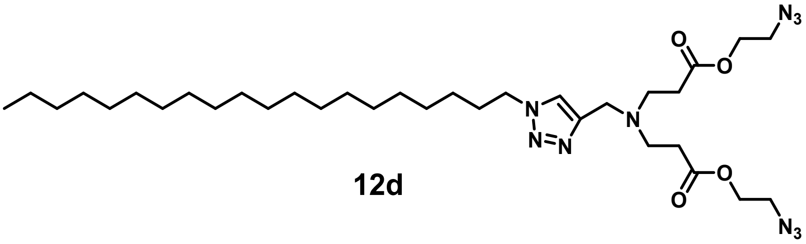
12b

12b: Colorless oil; yield: 88.9 mg (70%), prepared according to the general procedure; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 1H), 4.34 (t, *J* = 7.5 Hz, 2H), 4.27 (t, *J* = 4.5 Hz, 4H), 3.84 (s, 1H), 3.50 (t, *J* = 4.5 Hz, 2H), 2.85 (t, *J* = 6.0 Hz, 4H), 2.58 (t, *J* = 6.0 Hz, 4H), 1.91 (t, *J* = 7.5 Hz, 2H), 1.39 – 1.20 (m, 26H), 0.90 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.09, 144.29, 122.45, 63.01, 50.39, 49.78, 48.86, 48.48, 32.69, 31.98, 30.38, 29.74, 29.71, 29.67, 29.60, 29.46, 29.42, 29.08, 26.57, 22.75, 14.20. IR (cm^{-1}): *υ* 2101.97 ($-N_3$).



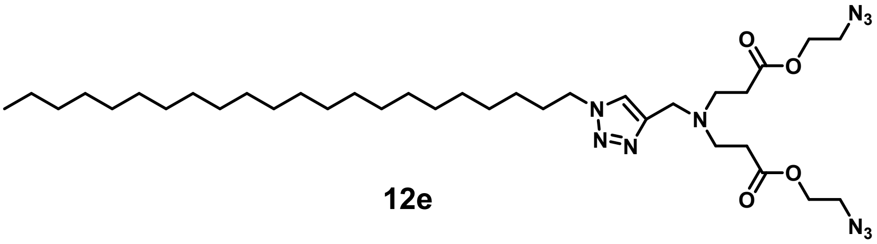
12c

12c: Colorless oil liquid; Yield – (114.3 mg, 86%); prepared as shown in the general experimental procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.45 (s, 1H), 4.32 (t, *J* = 7.3 Hz, 2H), 4.24 (t, *J* = 5.1 Hz, 4H), 3.82 (s, 2H), 3.48 (t, *J* = 5.1 Hz, 4H), 2.83 (t, *J* = 7.0 Hz, 4H), 2.56 (t, *J* = 7.0 Hz, 4H), 1.98 – 1.80 (m, 2H), 1.41 – 1.15 (m, 30H), 0.88 (t, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 172.18, 144.40, 122.46, 63.07, 50.45, 49.84, 48.92, 48.54, 32.78, 32.05, 30.44, 29.82, 29.78, 29.74, 29.67, 29.53, 29.49, 29.14, 26.64, 22.82, 14.26. IR (cm^{-1}): *υ* 2102.53 (-N$_3$).



12d

12d: Colorless oil; yield: 114.3 mg (86%), prepared according to the general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.45 (s, 1H), 4.32 (t, *J* = 7.5 Hz, 2H), 4.24 (t, *J* = 6.0 Hz, 4H), 3.82 (s, 1H), 3.48 (t, *J* = 6.0 Hz, 2H), 2.83 (t, *J* = 7.5 Hz, 4H), 2.56 (t, *J* = 7.5 Hz, 4H), 1.89 (t, *J* = 7.5 Hz, 2H), 1.37 – 1.16 (m, 34H), 0.87 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$) δ 172.12, 144.37, 122.43, 63.01, 50.40, 49.81, 48.92, 48.52, 32.76, 32.00, 30.39, 29.78, 29.70, 29.62, 29.49, 29.44, 29.10, 26.60, 22.77, 14.20. IR (cm^{-1}): *υ* 2104.59 (-N$_3$).



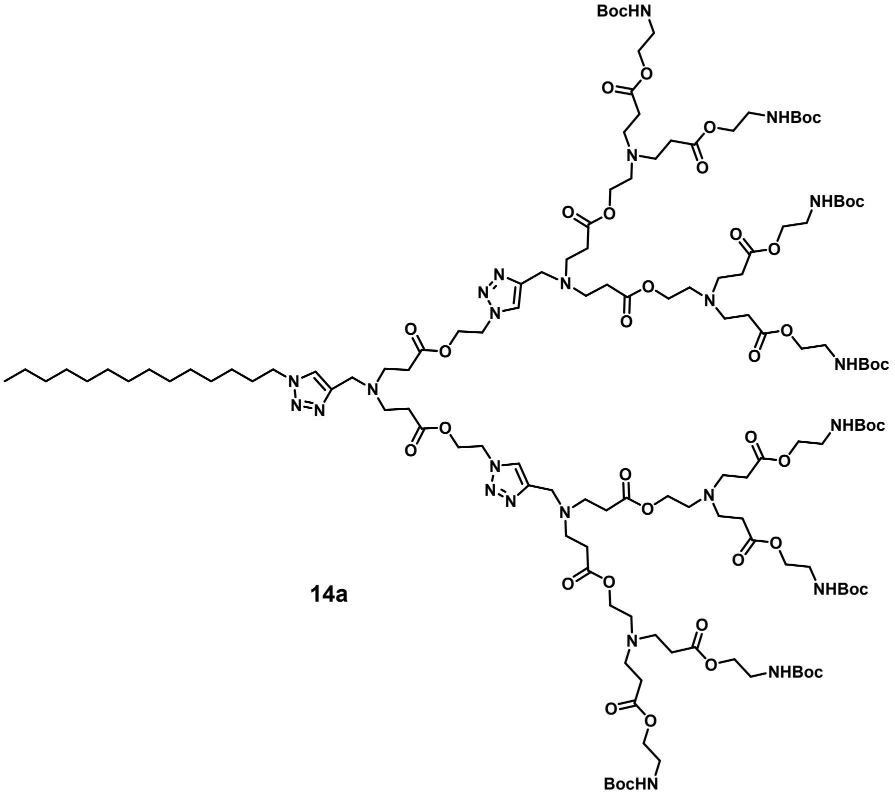
12e

12e: Colorless oil; yield: 104.2 mg (72%), prepared according to the general procedure; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.45 (s, 1H), 4.33 (t, *J* = 7.5 Hz, 2H), 4.25 (t, *J* = 4.5 Hz, 4H), 3.82 (s, 1H), 3.48 (t, *J* = 4.5 Hz, 2H), 2.83 (t, *J* = 7.5 Hz, 4H), 2.56 (t, *J* = 6.0

Hz, 4H), 1.87 (t, *J* = 3.0 Hz, 2H), 1.39 – 1.16 (m, 38H), 0.88 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.15, 144.34, 122.46, 63.05, 50.42, 49.81, 48.90, 48.51, 32.74, 32.02, 30.41, 29.80, 29.76, 29.72, 29.64, 29.51, 29.46, 29.12, 26.61,22.79, 14.23. IR (cm^{-1}): *υ* 2103.95 (-N_3).

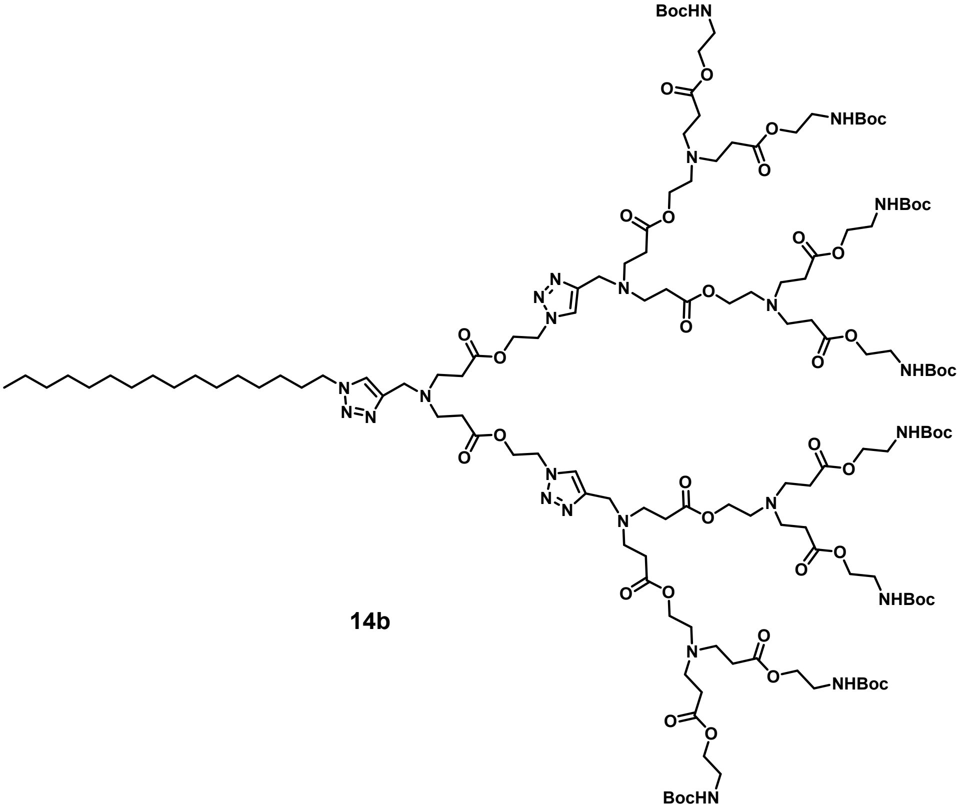
Synthesis and characterization of 14

Under an argon atmosphere, compound **12** (0.025 mmol, 1.0 equiv.), $CuSO_4·5H_2O$ (0.013 mmol, 0.5 equiv.), and sodium ascorbate (0.025 mmol, 1.0 equiv.) were dissolved in DMF (4.0 mL). A solution of dendron **13** (0.052 mmol, 2.1 equiv.) was added dropwise at 0°C. The reaction mixture was stirred at 50°C for 3 h in the dark. After removal of the solvent under reduced pressure, the crude product was diluted with DCM (30 mL), washed sequentially with saturated NH_4Cl solution (30 mL × 3) and saturated NaCl solution (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (DCM/EtOH = 15/1 to 10/1) afforded compound **14a-2** as colorless oils.



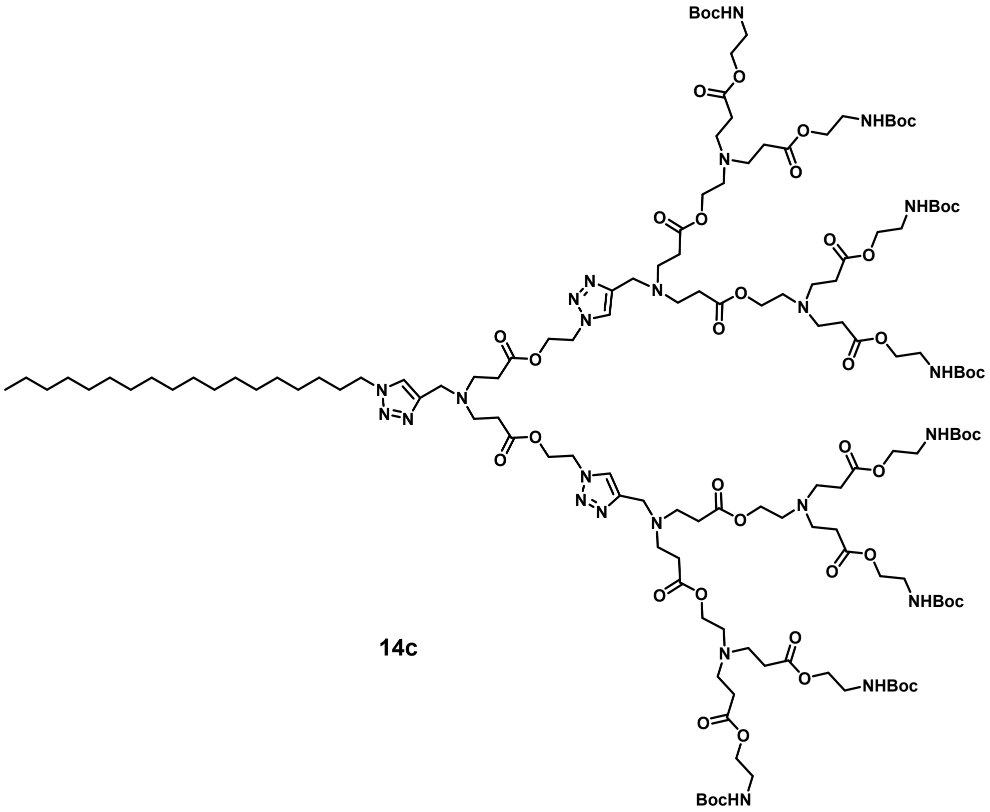
14a

14a: Colorless oil; yield: 51.0 mg (71%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (s, 2H), 7.50 (s, 1H), 4.62 (t, *J* = 5.3 Hz, 4H), 4.47 (t, *J* = 5.3 Hz, 4H), 4.34 (t, *J* = 7.3 Hz, 2H), 4.20 – 4.04 (m, 24H), 3.81 (s, 4H), 3.75 (s, 2H), 3.38 (d, *J* = 3.0 Hz, 16H), 2.95 – 2.63 (m, 36H), 2.60 – 2.36 (m, 28H), 1.95 – 1.85 (m, 2H), 1.44 (s, 72H), 1.34 – 1.20 (m, 22H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.30, 172.25, 171.88, 155.88, 144.48, 143.61, 123.38, 122.60, 79.37, 63.65, 62.36, 62.19, 52.00, 50.29, 49.78, 48.91, 48.68, 48.59, 48.21, 47.87, 39.57, 32.82, 32.53, 32.44, 31.87, 30.33, 29.64, 29.60, 29.51, 29.40, 29.31, 29.01, 28.38, 26.51, 22.65, 14.11.



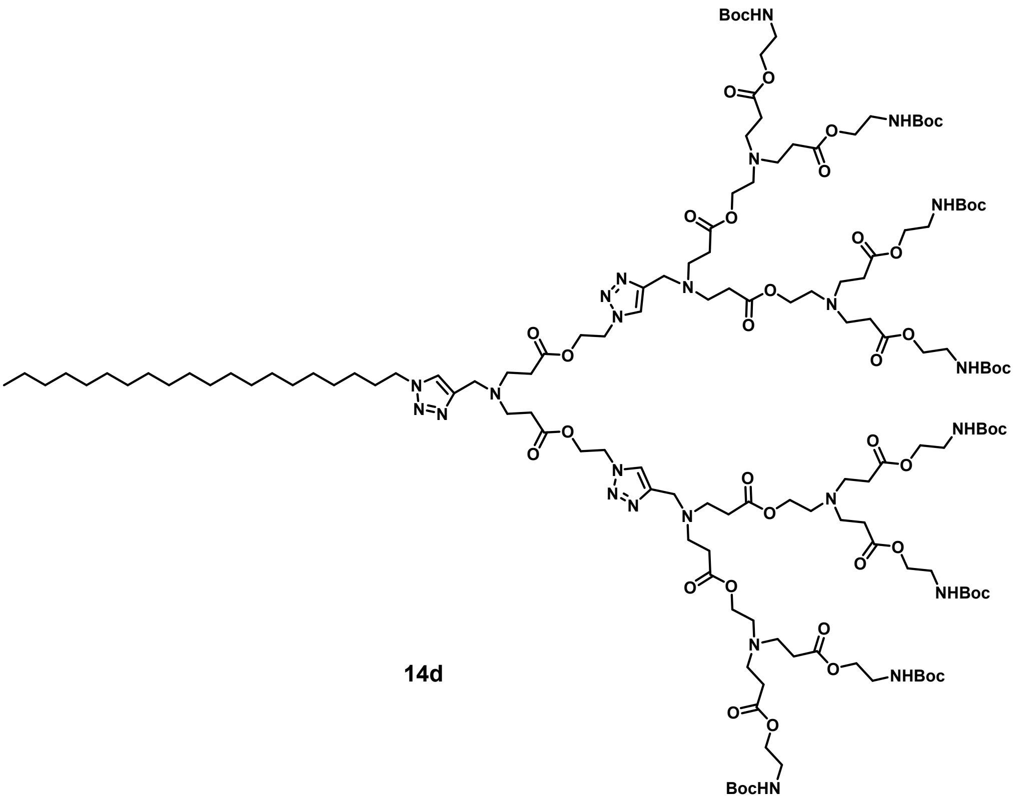
14b

14b: Colorless oil; yield: 55.0 mg (75%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66 (s, 2H), 7.50 (s, 1H), 4.62 (t, *J* = 5.3 Hz, 4H), 4.47 (t, *J* = 5.3 Hz, 4H), 4.34 (t, *J* = 7.4 Hz, 2H), 4.22 – 4.02 (m, 24H), 3.81 (s, 4H), 3.76 (s, 2H), 3.38 (s, 16H), 3.03 – 2.63 (m, 36H), 2.62 – 2.33 (m, 28H), 1.95 – 1.84 (m, 2H), 1.44 (s, 72H), 1.35 – 1.09 (m, 26H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.25, 172.21, 171.82, 155.84, 144.40, 143.39, 123.41, 122.61, 79.28, 63.57, 62.30, 62.13, 51.93, 50.25, 49.71, 48.87, 48.61, 48.51, 48.13, 47.79, 39.48, 32.74, 32.44, 32.35, 31.80, 30.25, 29.57, 29.53, 29.51, 29.45, 29.33, 29.24, 28.32, 26.43, 22.58, 14.04.



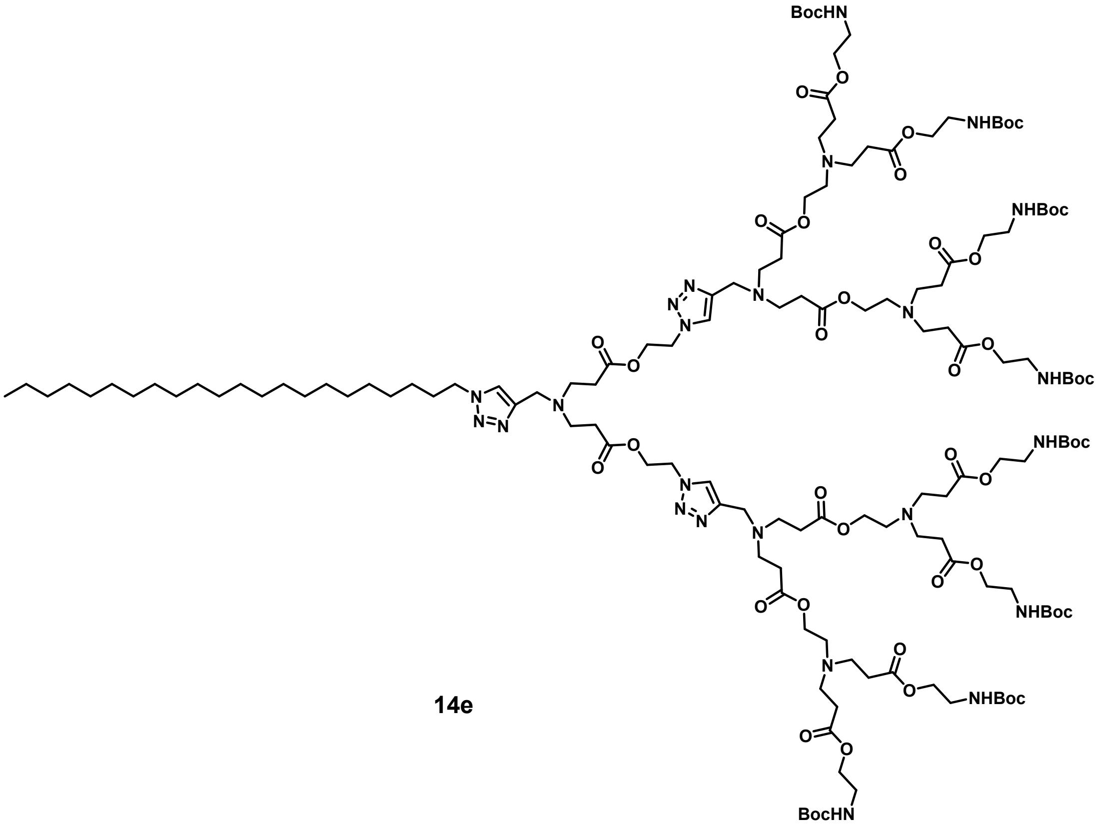
14c

14c: Colorless oil; yield: 54.9 mg (75%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 2H), 7.48 (s, 1H), 4.62 (t, *J* = 5.3 Hz, 4H), 4.46 (t, *J* = 5.2 Hz, 4H), 4.33 (t, *J* = 7.3 Hz, 2H), 4.22 – 4.02 (m, 24H), 3.80 (s, 4H), 3.75 (s, 2H), 3.38 (q, *J* = 4.9 Hz, 16H), 2.95 – 2.62 (m, 36H), 2.60 – 2.34 (m, 28H), 1.96 – 1.81 (m, 2H), 1.43 (s, 72H), 1.33 – 1.17 (m, 30H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.41, 172.37, 171.98, 155.96, 144.50, 143.64, 123.52, 122.70, 79.50, 63.75, 62.45, 62.26, 52.04, 50.40, 49.82, 48.99, 48.70, 48.61, 48.25, 47.91, 39.62, 32.86, 32.52, 32.46, 31.97, 30.42, 29.75, 29.71, 29.63, 29.51, 29.41, 29.11, 28.46, 26.60, 22.74, 14.20.



14d

14d: Colorless oil; yield: 47.9 mg (75%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 2H), 7.49 (s, 1H), 4.62 (t, *J* = 5.4 Hz, 4H), 4.47 (t, *J* = 5.4 Hz, 4H), 4.34 (t, *J* = 7.3 Hz, 2H), 4.20 – 4.06 (m, 24H), 3.81 (s, 4H), 3.76 (s, 2H), 3.38 (q, *J* = 5.5 Hz, 16H), 2.91 – 2.66 (m, 36H), 2.58 – 2.38 (m, 28H), 1.97 – 1.84 (m, 2H), 1.44 (s, 72H), 1.38 – 1.14 (m, 34H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.28, 172.24, 171.86, 155.87, 144.51, 143.68, 123.39, 122.60, 79.36, 63.64, 62.35, 62.19, 51.99, 50.32, 49.77, 48.93, 48.68, 48.59, 48.22, 47.89, 39.56, 32.82, 32.51, 32.42, 31.87, 30.31, 29.65, 29.60, 29.53, 29.41, 29.31, 29.01, 28.38, 26.51, 22.64, 14.10.

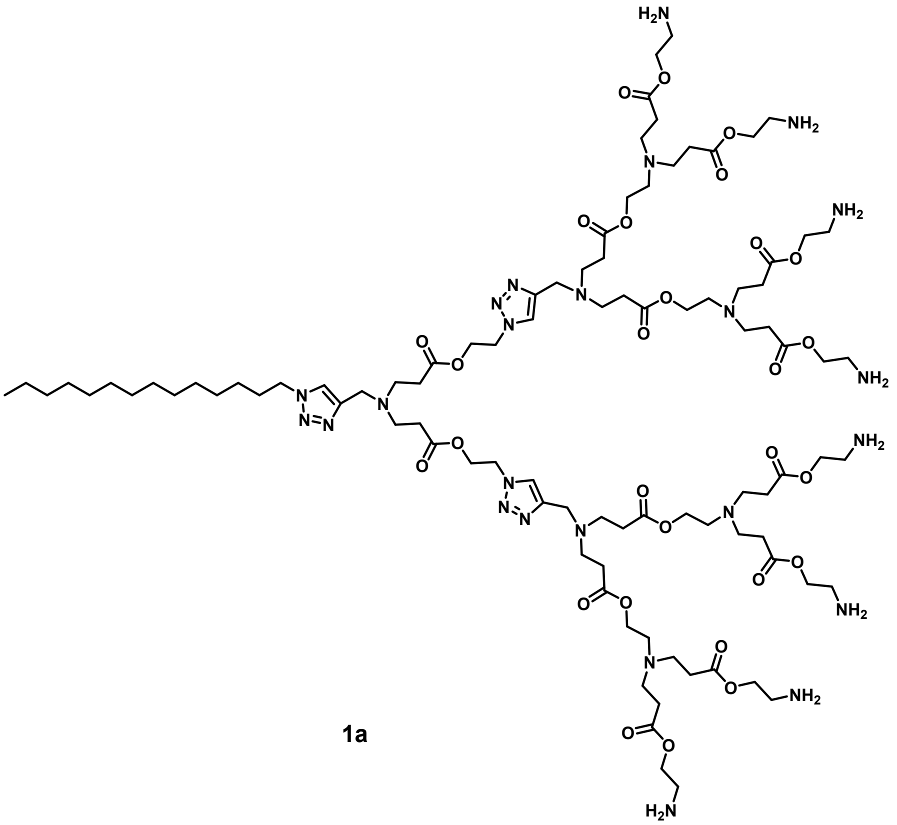


14e

14e: Colorless oil; yield: 58.1 mg (78%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (s, 2H), 7.49 (s, 1H), 4.62 (t, *J* = 5.2 Hz, 4H), 4.47 (t, *J* = 5.2 Hz, 4H), 4.34 (t, *J* = 7.4 Hz, 2H), 4.22 – 4.04 (m, 24H), 3.81 (s, 4H), 3.76 (s, 2H), 3.39 (q, *J* = 5.5 Hz, 16H), 2.94 – 2.62 (m, 36H), 2.59 – 2.39 (m, 28H), 1.96 – 1.82 (m, 2H), 1.44 (s, 72H), 1.35 – 1.20 (m, 38H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.32, 172.27, 171.89, 155.90, 144.47, 143.60, 123.43, 122.63, 79.39, 63.66, 62.37, 62.20, 52.00, 50.31, 49.78, 48.93, 48.68, 48.58, 48.21, 47.87, 39.57, 32.82, 32.51, 32.43, 31.89, 30.34, 29.67, 29.62, 29.55, 29.43, 29.32, 29.03, 28.39, 26.52, 22.66, 14.11.

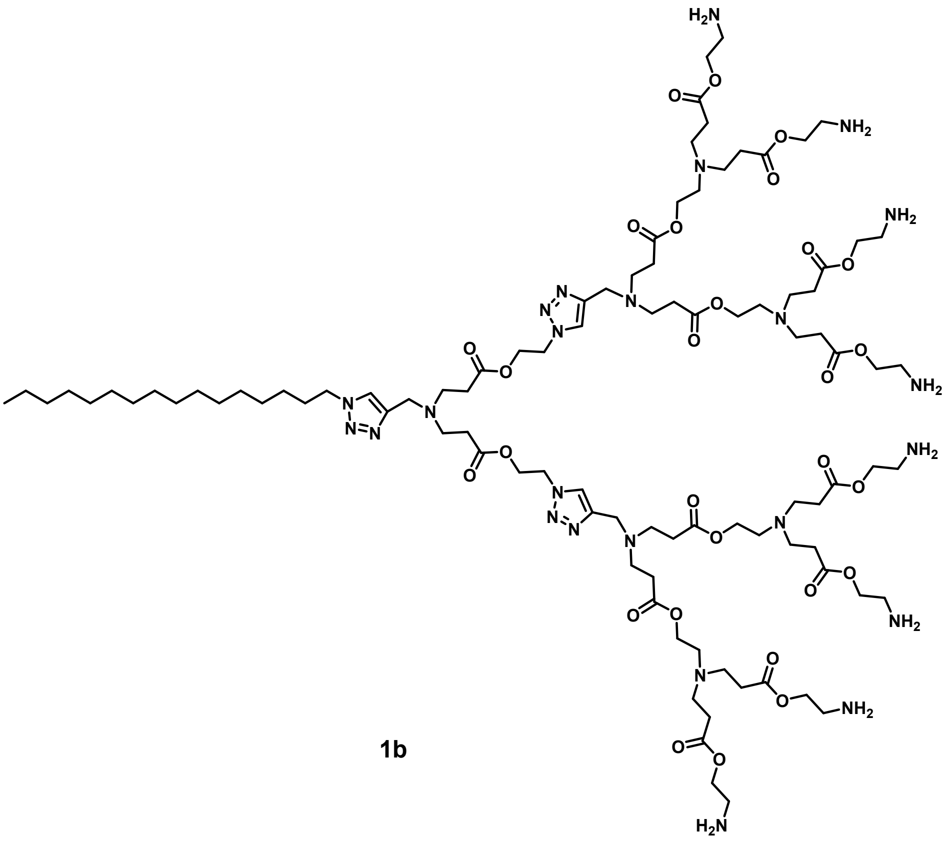
Synthesis and characterization of 1

Compound **14** (0.01 mmol, 1.0 equiv.) was dissolved in DCM (0.9 mL) under an argon atmosphere. TFA (4.2 mmol, 420.0 equiv.) was added dropwise at 0°C. The reaction mixture was stirred at 30°C for 3 h in the dark. After removal of solvents and reagents under reduced pressure, the deprotection procedure was repeated under the same conditions for an additional 3 h. The resulting residue was washed with anhydrous diethyl ether (10 mL × 3) to afford white solid **1**.



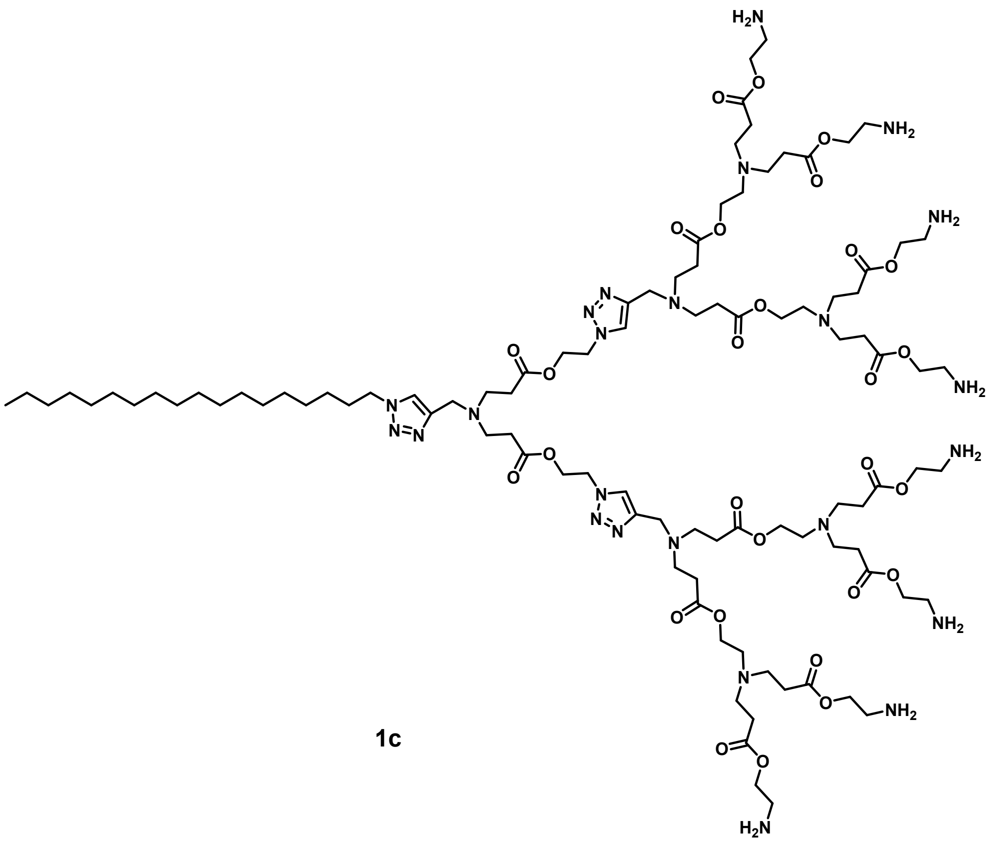
1a

1a: White solid; yield: 36.0 mg (95%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CD_3OD/CDCl_3 = 3/2$): δ 8.31 (s, 2H), 8.18 (s, 1H), 4.75 – 4.70 (m, 4H), 4.62 – 4.32 (m, 36H), 3.67 – 3.35 (m, 36H), 3.30 – 3.21 (m, 16H), 3.10 – 2.88 (m, 28H), 1.99 – 1.88 (m, 2H), 1.41 – 1.19 (m, 22H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CD_3OD/CDCl_3 = 3/2$): δ 169.96, 169.49, 135.39, 135.08, 127.44, 79.37, 62.58, 60.79, 58.58, 51.69, 50.07, 48.85, 48.73, 48.33, 48.12, 47.90, 47.69, 47.48, 47.26, 47.05, 46.50, 37.94, 31.24, 29.46, 28.98, 28.96, 28.94, 28.87, 28.74, 28.65, 28.33, 27.99, 27.90, 27.70, 25.76, 21.95, 13.00. ESI-MS calcd for $C_{95}H_{170}N_{24}O_{28}$ $[M+H]^+$ 2069.2410, found 2069.2345 (-2.97 ppm).



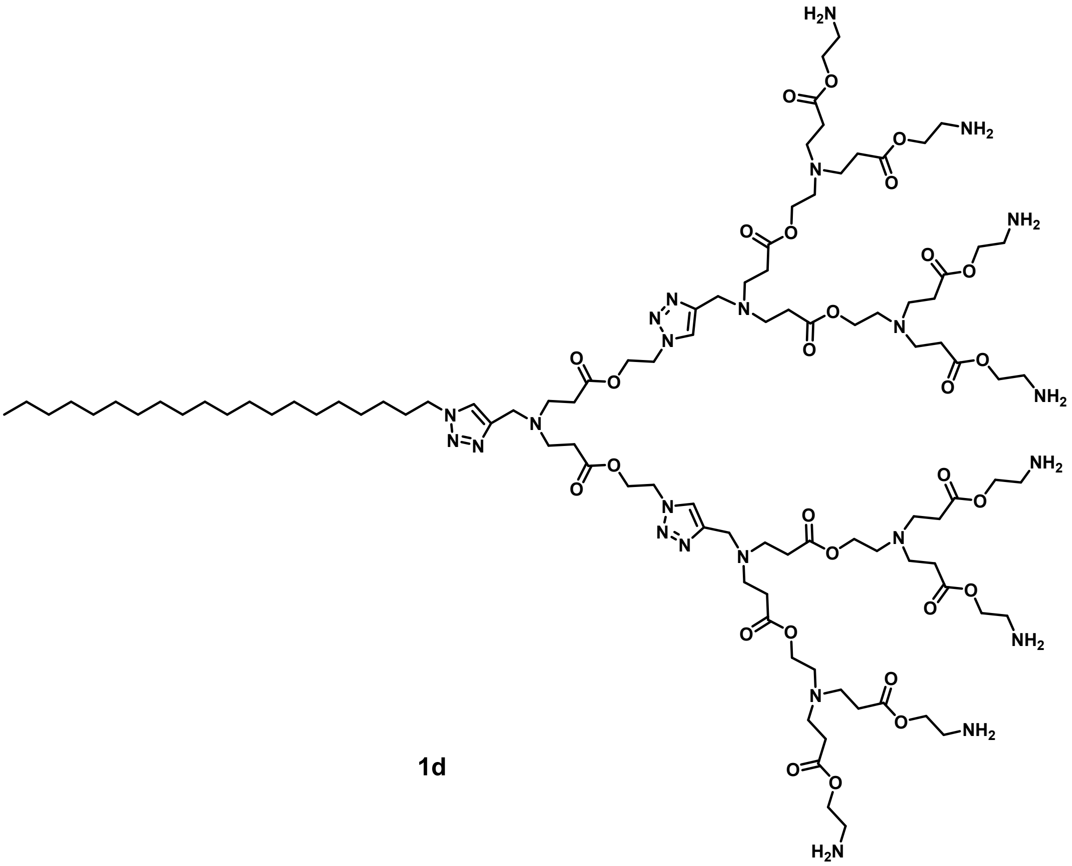
1b

1b: White solid; yield: 38.0 mg (96%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CD_3OD/CDCl_3 = 3/2$): δ 8.32 (s, 2H), 8.18 (s, 1H), 4.75 – 4.70 (m, 4H), 4.61 – 4.30 (m, 36H), 3.70 – 3.36 (m, 36H), 3.29 – 3.19 (m, 16H), 3.07 – 2.88 (m, 28H), 1.98 – 1.87 (m, 2H), 1.43 – 1.17 (m, 26H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CD_3OD/CDCl_3 = 3/2$): δ 169.98, 169.51, 135.41, 135.08, 127.45, 79.28, 62.60, 60.80, 58.60, 51.71, 50.09, 48.87, 48.75, 48.33, 48.12, 47.90, 47.69, 47.48, 47.27, 47.05, 46.52, 37.95, 31.27, 29.49, 29.00, 28.97, 28.90, 28.77, 28.68, 28.36, 28.00, 27.91, 27.72, 27.68, 25.78, 21.98, 13.03. ESI-MS calcd for $C_{95}H_{170}N_{24}O_{28}$ $[M+H]^+$ 2097.2723, $[M+Na]^+$ 2119.2542, found 2097.2686 (-1.76 ppm), 2119.2479 (-2.97 ppm).



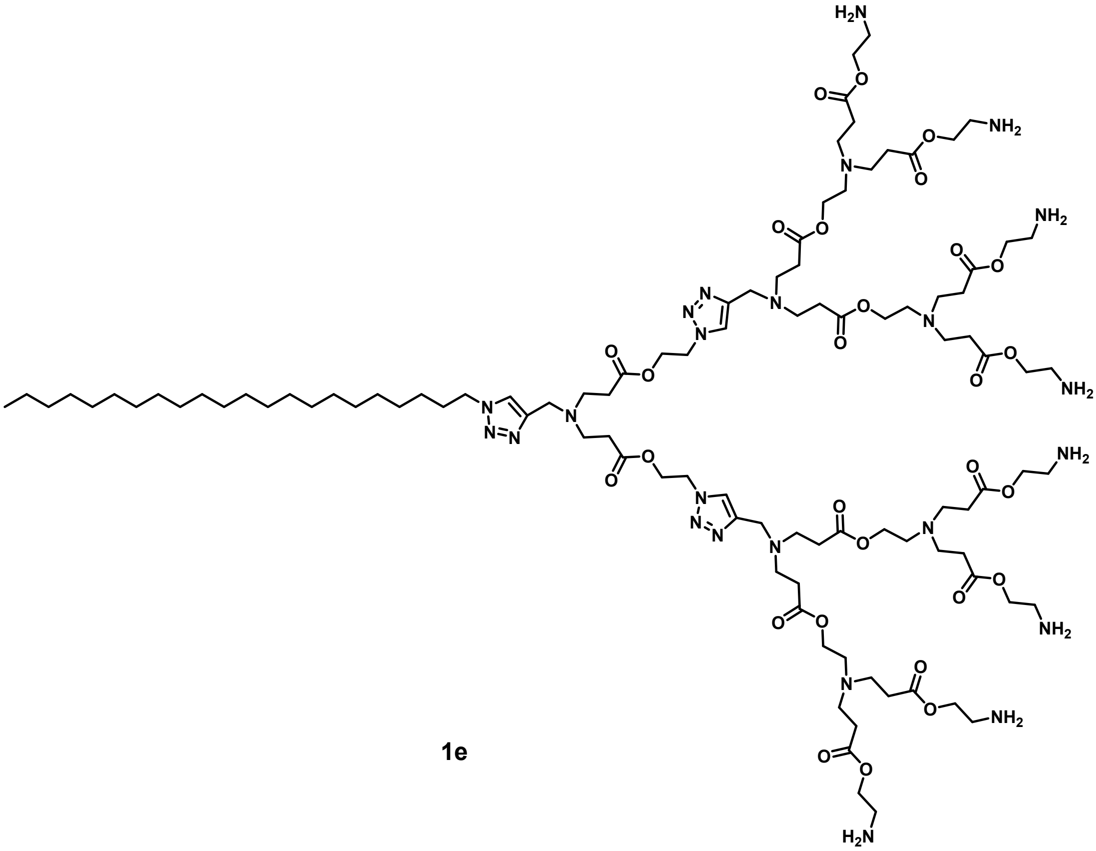
1c

1c: White solid; yield: 38.0 mg (96%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CD_3OD/CDCl_3$ = 3/2) δ 8.31 (s, 2H), 8.18 (s, 1H), 4.75 – 4.70 (m, 4H), 4.65 – 4.28 (m, 36H), 3.65 – 3.35 (m, 36H), 3.26 (t, *J* = 5.1 Hz, 16H), 3.14 – 2.85 (m, 28H), 2.01 – 1.86 (m, 2H), 1.43 – 1.19 (m, 30H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CD_3OD/CDCl_3$ = 3/2) δ 171.26, 170.81, 136.76, 128.65, 127.84, 63.83, 62.06, 59.93, 53.01, 51.46, 50.38, 50.17, 50.06, 47.86, 47.74, 39.24, 32.54, 30.74, 30.27, 30.24, 30.18, 30.05, 29.95, 29.63, 29.40, 29.38, 29.26, 29.10, 29.00, 27.08, 23.25, 14.31. ESI-MS calcd for $C_{97}H_{174}N_{24}O_{28}$ $[M+H]^+$ 2125.3036, found 2125.3034 (-0.09 ppm).



1d

1d: White solid; yield: 38.0 mg (96%), prepared according to the general procedure; ^{1}H NMR (300 MHz, $CD_3OD/CDCl_3 = 3/2$) δ 8.33 (s, 2H), 8.19 (s, 1H), 4.75 – 4.70 (m, 4H), 4.66 – 4.21 (m, 36H), 3.65 – 3.35 (m, 36H), 3.31 – 3.21 (m, 16H), 3.13 – 2.85 (m, 28H), 1.98 – 1.88 (m, 2H), 1.43 – 1.16 (m, 26H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CD_3OD/CDCl_3 = 3/2$) δ 169.98, 169.51, 135.39, 135.02, 127.50, 126.52, 79.36, 62.60, 60.82, 58.59, 51.71, 50.12, 48.86, 48.36, 48.14, 47.93, 47.72, 47.50, 47.29, 47.08, 46.52, 37.96, 31.27, 29.48, 29.38, 29.01, 28.97, 28.92, 28.79, 28.68, 28.37, 27.99, 27.70, 27.65, 25.80, 21.98, 13.04. ESI-MS calcd for $C_{99}H_{178}N_{24}O_{28}$ [M+H]$^+$ 2153.3349, found 2153.3298 (-2.4 ppm).



1e

1e: White solid; yield: 38.0 mg (96%), prepared according to the general procedure; ^{1}H NMR (300 MHz, CD$_3$OD/CDCl$_3$ = 3/2) δ 8.31 (s, 2H), 8.17 (s, 1H), 4.75 – 4.70 (m, 4H), 4.68 – 4.26 (m, 36H), 3.67 – 3.34 (m, 36H), 3.31 – 3.19 (m, 16H), 3.14 – 2.78 (m, 28H), 1.98 – 1.88 (m, 2H), 1.42 – 1.19 (m, 38H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, CD$_3$OD/CDCl$_3$ = 3/2) δ170.00, 169.53, 135.46, 135.08, 127.46, 126.51, 79.39, 62.61, 60.81, 58.62, 51.73, 50.12, 48.88, 48.36, 48.15, 47.93, 47.72, 47.51, 47.29, 47.08, 46.52, 37.97, 31.30, 29.51, 29.05, 29.02, 28.99, 28.95, 28.82, 28.71, 28.39, 28.04, 27.95, 27.76, 25.82, 22.01, 13.06. ESI-MS calcd for $C_{101}H_{182}N_{24}O_{28}$ [M+H]$^+$ 2181.3662, found 2181.3531 (-6.0 ppm).

Degradation measurement of dendrimers (1a-1e)

PAE dendrimers **I**, **I$_0$** and **1a-1e** were each dissolved in ultrapure water to prepare 0.3 mM solutions and then incubated at 25°C. As an example, the aqueous solution of 1c was also incubated at 37 °C. Degradation was monitored at predetermined time points (0, 1, 2, 3, 4, 8, 12 and 24 h) by high-performance liquid chromatography (HPLC). The degradation rate (υ) was calculated based on the reduction of the main chromatographic peak area according to the equation:

$$v = \frac{A_{(0)} - A_{(t)}}{A_{(0)}} \times 100\%$$

Where $A_{(t)}$ and $A_{(0)}$ represent the peak areas at time (t) and initial time 0, respectively. Degradation profiles were plotted as degradation rate versus time for all dendrimers

Critical aggregation concentration (CAC) determination

The CAC of amphiphilic PAE dendrimers was determined using Nile red florescence probes. A 2.5 mM Nile Red stock solution was prepared in ethanol. Amphiphilic PAE dendrimer solutions were prepared in pH 7.4 phosphate buffer (PB) at concentrations ranging from 0.1 to 400 µM. To each milliliter of dendrimer solution, 1 µL of Nile Red stock was added to yield a final Nile Red concentration of 2.5 nM. Samples were sonicated for 10 min in the dark and then incubated at room temperature in the dark for 2 h. Aliquots (150 µL) were dispensed in triplicate into 96-well plates. Fluorescence measurements were performed using a multifunctional enzyme marker with excitation at 550 nm and emission at 635 nm. The fluorescence intensity was plotted against dendrimer concentration to determine the CAC.

Cell culture

Human normal liver L02 cells, mouse fibroblast L929 cells, and Madin-Darby canine kidney (MDCK) cells were obtained from Tongpai Biotechnology Co., Ltd. (Shanghai, China). L02 and L929 cells were cultured in RPMI-1640 medium (Hyclone, Utah, USA) supplemented with 10% fetal bovine serum (FBS). MDCK cells were maintained in MEM (Hyclone) with 10% FBS. All cells were incubated at 37 °C in a humidified atmosphere containing 5% CO_2.

MTT assay

Normal cell lines (L929, MDCK, and L02) were seeded in 96-well plates at a density of 8.0×10^3 cells per well and allowed to adhere overnight. Amphiphilic PAE dendrimer solutions were prepared in serum-free medium at concentrations of 1, 5, 10, 20, 40, 50, 75, and 100 µM and added to the cells. After incubation for 8 h at 37 °C, the treatment medium was replaced with complete medium containing 10% fetal bovine serum (FBS), and cells were further incubated for 48 h. Subsequently, 10 µL of MTT solution (0.5 mg/mL in PBS) was added to each well, and the plates were incubated at 37 °C for 4 h. The supernatants were then carefully removed, and 100 µL of dimethyl sulfoxide (DMSO) was added to each well to dissolve the formazan crystals. The absorbance was measured at 540 nm using a microplate reader. Cell viability was calculated relative to untreated controls.

Statistical tests

All data are presented as mean ± standard deviation (SD) unless otherwise indicated.

References

1. C. Bouillon, G. Quelever and L. Peng, *Tetrahedron Lett.*, 2009, **50**, 4346.
2. C. Bouillon, A. Tintaru, V. Monnier, L. Charles, G. Quéléver and L. Peng, *J. Org. Chem*., 2010, **75**, 8685–8688.
3. C. Ma, D. Zhu, W. Lin, Y. Li, Y. Huang, H. Zhu, M. Ye, Y. Wang, L. Peng and X. Liu, *Chem. Commun.*, 2022, **58**, 4168.